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# A SYSTEM OF MEDICINE

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M.D., F.R.S., and H. D. ROLLESTON, M.D., F.R.C.P.*

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# SYSTEM OF MEDICINE

BY MANY WRITERS



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VOLUME VII

DISEASES OF THE MUSCLES, THE TROPHONEUROSES, DISEASES OF  
THE NERVES, VERTEBRAL COLUMN, AND SPINAL CORD

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## PREFACE

OF the contents of the present volume, the Diseases of Muscles, the Trophoneuroses, the Diseases of Nerves and of the Vertebral Column and its membranes were included in Volume VI. of the original edition, whilst the Diseases of the Spinal Cord occupied the early part of Volume VII. The next volume (VIII.) of the present edition contains the Diseases of the Brain and Mental Diseases; and the final volume (IX.) is devoted to Diseases of the Skin. It is hoped that this re-arrangement will be an advantage to readers.

Extensive changes have been made in this volume; the section on Diseases of Muscles has been considerably enlarged, more freely illustrated, and reinforced by additional articles on Amyotonia Congenita (Dr. James Collier), Myasthenia Gravis (Dr. Farquhar Buzzard), Family Periodic Paralysis (Prof. J. Michell Clarke), and the Neuritic Type of Progressive Muscular Atrophy (Dr. F. E. Batten). The late Dr. C. E. Beevor's article on Myopathy has been revised by Dr. F. E. Batten. Dr. Turney has expanded his article on the Trophoneuroses by the inclusion of the affections of soft parts, a subject treated in a separate article in the first edition.

The advances of Neurology during the past ten years are reflected in the numerous changes necessitated in the Section on Diseases of the Nervous System. Dr. Mott's authoritative and admirably illustrated "Introduction to Neuro-pathology" is an

entirely new articles, as is Sir William Gowers' contribution on Medical Ophthalmology. In the section on Diseases of the Nerves new articles will be found on Diseases of the Cauda Equina (Dr. R. A. Fleming), and on Diseases of the Sympathetic System (Dr. Gordon M. Holmes). The article on Herpes Zoster, formerly placed among Diseases of the Skin, has now been included here.

The article on Myelitis has been completely re-written, and Dr. Farquhar Buzzard has provided an account of Landry's Paralysis. Dr. Leonard Hill has supplied a new article on Caisson Disease, and Dr. Purves Stewart a fresh account of Senile Paraplegia. There are additional articles dealing with Subacute Combined Degeneration of the spinal cord (Dr. James Collier), Familial and Hereditary Ataxia (Dr. Gordon M. Holmes), Syphilis (Dr. Wilfred Harris), and Tumours of the Spinal Cord (Dr. Edwin Bramwell). Under the heading of "Motor Neuron Disease" Dr. Batten and Dr. Gordon M. Holmes have re-arranged and revised the late Dr. C. E. Beevor's articles on Chronic Anterior Poliomyelitis and Amyotrophic Lateral Sclerosis.

The Editors are indebted to Dr. Henry Head for much generous help and advice, and to Dr. A. J. Jex-Blake for a number of corrections in the text.

CLIFFORD ALLBUTT.

H. D. ROLLESTON.

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*In order to avoid frequent interruption of the text, the numbers indicative of items in the lists of "References" are only inserted in cases of emphasis, where two or more references to the same author are in the list, where an author is quoted from a work published under another name, or where an authoritative statement is made without mention of the author's name. In ordinary cases an author's name is sufficient indication of the corresponding item in the list.*

## DISEASES OF THE MUSCLES

MYOSITIS.

AMYOTONIA CONGENITA.

MYOTONIA CONGENITA.

MYOPATHY.

MYASTHENIA GRAVIS.

FAMILY PERIODIC PARALYSIS.

---

NEURITIC TYPE OF PROGRESSIVE  
MUSCULAR ATROPHY.



## MYOSITIS

By FREDERICK E. BATTEN, M.D., F.R.C.P.

THE classification of the various inflammatory conditions of muscles presents considerable difficulty. Lorenz divides them into the two great groups, suppurative and non-suppurative, and adds a third to include myositis ossificans and myositis fibrosa. The following classification, used in the last edition of this work, is to my mind the most suitable:—

(A) *Primary Affections of Muscles.*

(a) Polymyositis—including acute polymyositis, dermato-myositis, haemorrhagic myositis, polymyositis with erythema multiforme and urticaria, and pseudo-trichinosis.

(b) Neuro-myositis.

(c) Tuberculous myositis.

(d) Syphilitic myositis: (a) diffuse; (β) gumma of muscle.

(e) Myositis due to *Trichinella spiralis* (see Art. Vol. II. Part II. p. 908).

(B) *Secondary Affections of Muscles* in the course of some acute or chronic disease; the resulting condition may be either general or local, parenchymatous or interstitial, suppurative or non-suppurative.

(a) Myositis in the course of specific fevers, such as enteric, typhus, small-pox.

(b) Infective myositis, occurring in pyaemia, puerperal infection, infective endocarditis, glanders, infected wounds, actinomycesis, erysipelas, and gonorrhoea.

(C) *Myositis with Special Terminal Lesions.*

(a) Myositis ossificans: (a) local ossification; (β) myositis ossificans progressiva.

(b) Myositis fibrosa; (a) local; (b) general.

A. PRIMARY AFFECTIONS OF THE MUSCLES.—(a) **Acute Polymyositis.**—The characteristic features of this disease, also known as dermato-myositis and pseudo-trichinosis, have been defined during recent years.

In 1887 Unverricht, Hepp, and Wagner recorded cases of this nature, Hepp's case being published under the title of pseudo-trichinosis.

Strümpell, in 1891, described another case, with necropsy, and summed up the leading features of the disease. Since that date several cases with necropsies have been reported, and, according to Lorenz, 15 undoubted examples of polymyositis with the characteristics of dermato-myositis are on record.

*Etiology.*—The causation is obscure. Neither of the two hypotheses, (i.) that the disease is due to a toxin, and (ii.) that it depends on an animal parasite belonging to the order of the Gregarinoidea, has been proved. It is possible that some of the cases may have been due to *Trichinella spiralis* (Wagner's case); but such cases should obviously be excluded from this group. Careful examination of the muscles has given a negative result, both bacteriologically and as regards *Trichinella spiralis*.

The suggestion that the condition is due to a toxin derived from the ingesta receives some support from the cases observed by Senator and by Kell; for in the case reported by the former the disease followed the eating of some stale crabs, and in the latter the ingestion of a fish, by which three persons were said to have been infected, one of whom died. In Senator's case the disease did not appear till some time after the crabs were eaten; whereas in Kell's cases it came on within a few hours, though the cases were not simultaneous; the case in which symptoms appeared first proved fatal.

The suggestion that the disease is due to a gregarine is based on the occurrence in the lower animals of myositis due to a protozoon, a sporozoon belonging to the order Gregarinoidea; and it is also stated that in a hog affected with gregarinal myositis, Virchow observed a skin lesion very similar to that seen in the acute polymyositis of man. In this connexion, however, the researches of Pluymsers on the Sarcosporidia (*vide* also Vol. II. Part II. p. 103) may be of interest as shewing how small may be the irritation to which they may give rise.

The disease has supervened in the course of diabetes, tuberculous disease of the lungs and of the intestines, and after injury to the tongue. Litten and Sölders have shewn that a form of myositis occurs after poisoning with carbonic oxide. Myositis due to syphilis should not be classed under this heading.

There is no evidence that the disease is contagious, except perhaps that brought forward by Lewy, the nature of whose cases may well be called in question.

*Age and Sex.*—Out of the 11 cases collected by Pfeiffer, 4 were women and 7 were men. The youngest patient was seventeen, and the oldest a man seventy years of age. Schüller published a case of polymyositis in a boy seven years old, and has collected other cases of a similar kind.

*Pathology.*—Almost any or all the muscles of the body may be affected, but the masseters and the ocular muscles usually escape. The muscular tissue is swollen and of a yellowish-white colour, and appears covered with brownish-red patches. Haemorrhages can be seen in the muscle. Sometimes the most striking feature about the muscle is its soft and friable state. Microscopical examination shews both a

parenchymatous and interstitial inflammatory condition of the muscle, which may be either focal or diffuse. The muscle-fibres are swollen and granular, and for the most part have lost their striation, often presenting a hyaline or waxy degeneration; vacuoles are present, but there is no proof that fatty degeneration occurs. Increase of round cells between the fibres is always present, and haemorrhages can be seen in this situation. The greatest amount of infiltration is found in the neighbourhood of the vessels. From a digest of the various cases, Pfeiffer concludes that the disease is primarily an affection of the connective tissue, and that the muscle-fibres suffer secondarily. The heart-muscle was found involved in one case. No change is found in the brain, spinal cord, or in the peripheral nerves. There is often a pneumonic condition of the lungs. The spleen is enlarged and soft.

*Symptoms.*—The disease is characterised by swelling of the extremities, due to an inflammatory oedema of the subcutaneous tissue and the muscles, acute pain, muscular rigidity, great tenderness on pressure, and an erythematous rash, resembling erysipelas, situated over the affected muscles. The character of the rash may vary to a very great extent; it may resemble urticaria, erythema nodosum, or purpura.

The onset of the disease is gradual, with malaise, weakness, loss of appetite, headache, and sometimes vomiting. There is usually a moderate rise of temperature, but rigors are absent, and the local symptoms appear later, with acute pain resembling cramp, and tenderness beginning usually in the legs or arms. At the commencement of the illness the pain is not generally so severe as to prevent movement of the limbs; later, however, the least movement causes so much pain that the patient lies helpless in bed. Other muscles of the body may become affected—the diaphragm, the intercostals, and the muscles of deglutition—so that the patient has great difficulty in speaking and swallowing. The tongue and the ocular muscles have been affected in some cases. Sensation is perfectly preserved, and the nerves are not tender on pressure. The joints are unaffected. The knee-jerks are generally present, though the swollen condition of the limb and the pain caused by percussion may make it somewhat difficult to obtain them. The electrical reactions in this stage of the disease, when tested, have been found to be normal. Stomatitis and throat affections may occur either early or late in the disease. The urine is generally normal, but it may contain some albumin. The spleen is commonly enlarged. The course of the disease tends in the slighter cases to complete recovery after a duration of some weeks; in one case recovery took place in twelve days (Plehn). In the more severe forms recovery is often protracted; atrophy of the muscles follows the subsidence of the inflammation; electrical changes are found in the muscles; and well-marked pigmentation of the skin may be permanent. In Schüller's case of polymyositis in a boy, an attack of pertussis was followed by fever, dyspepsia, and a rash. After four days the initial symptoms passed off, but painful swellings appeared in the muscles of the face and neck. The trunk and proximal muscles were more affected than the distal. The



aeme of the disease was reached in three weeks, and in eight weeks the boy was well.

The most severe cases end fatally from implication of the muscles of respiration or from secondary affections of the lungs, such as bronchitis or pneumonia.

That slighter forms of the disease exist which do not correspond in all particulars with the disease as above described is obvious from examination of the reported cases. The diagnosis of such cases will always be doubtful, for it is almost impossible to distinguish them from syphilitic or infective myositis, or from cases of slight trichinosis.

*Diagnosis.*—The disease, as above described, has certain definite features, namely, a gradual onset, attended by inflammatory swelling of the muscles, together with redness and swelling of the skin and subcutaneous tissue situated over the affected muscles, extreme tenderness, but no loss of sensation. It must, therefore, be distinguished from (i.) trichinosis. The presence of initial digestive disturbance and of considerable oedema of the face and eyelids early in the disease would point to infection by *Trichinella spiralis*; but the most certain test is the discovery of the *Trichinella* in the motions, or in an excised portion of the muscle; in late cases in which calcification of the sheath of the *Trichinella spiralis* has taken place a skiagram may be of service. The presence of a high grade of eosinophilia in a case of myositis would be very strong evidence in favour of trichinosis. (ii.) Neuro-myositis, in which the primary lesion is nervous. The more marked paralysis, the anaesthesia, the earlier and more rapid atrophy, the loss of knee-jerk, together with other evidence of nervous changes and the absence of the characteristic cutaneous affection, would point to a primary nerve-lesion. (iii.) Infective myositis. The presence of a focus of infection, and the positive bacteriological result on examination of the muscles, would distinguish this from acute polymyositis. (iv.) Syphilitic myositis.

*Prognosis*, both with regard to immediate recovery and also with regard to the subsequent effects of the disease, is by no means good. The disease in its severer forms is very fatal. In its less severe form it may lead to considerable muscular atrophy, and even in the slighter cases recovery may be prolonged.

The immediate *treatment* is confined to the relief of pain, the removal from the body of the source of irritation, and the nutrition of the patient. Later, the treatment should be directed to the bronchitis and pneumonia, and, as far as possible, to the prevention of muscular atrophy.

**Myositis Haemorrhagica.**—As very few examples of this condition have been recorded, the following description has been taken from that of a case recorded by Lorenz.

*Etiology.*—The cause of the disease is obscure, but in some instances the condition has come on after an acute infection of the throat.

*Morbid Anatomy.*—The muscles appear of a dirty-brown colour, and haemorrhagic foci can be seen between the muscular fasciculi. The myocardium shews the same brown colour, with small haemorrhages.



Microscopically during the acute stage intramuscular haemorrhages are found, the muscle-fibres being separated from one another by extravasated blood. The muscle-fibres have lost many of their nuclei, are vacuolated, and shew waxy degeneration. In the later stage the muscular fibres undergo extensive atrophy, the connective tissue is generally increased in amount, and blood-pigment is often present.

*Symptoms.*—The onset is acute, and attended by fever and by localised pain and swelling in the muscles, usually in the calf or thigh. The muscular swelling is hard and painful to the touch, and may be surrounded by oedema of the tissues. After a time these swellings disappear, while others rapidly appear elsewhere. The pain is very acute, and the movements of the limbs are greatly impaired. The skin is very liable to vasomotor disturbance, and any pressure may produce a bright-red spot, which persists for many minutes, or becomes purpuric.

Lorenz's patient, a man aged forty-three, previously in perfect health, was taken ill in December 1900 with pain in the left thigh; a small nodule could be felt in the muscle, which gradually increased in size for one week and then got smaller; after a time swellings occurred in other muscles, and the patient complained of difficulty in swallowing. Swellings could then be felt in various muscles, and were hard and painful on pressure. The heart shewed slight dilatation and irregularity. During the next month fresh swellings appeared in the muscles, the skin was very sensitive to any pressure, red spots being produced, which only disappeared after twenty to thirty minutes. The cardiac rhythm became more irregular, and attacks of tachycardia and dyspnoea supervened. The patient died at the end of June from cardiac failure. The muscles shewed evidence of both recent and old haemorrhages, and were of a greyish-brown colour. Haemorrhages both old and recent were present in the myocardium, but there was no valvular disease.

In contrast to this fatal case is the following case recorded by W. S. Thayer:—

A man aged thirty-four, who for fifteen years had suffered from "rheumatism," had for several years a series of attacks of swellings in various muscles. The amount of constitutional disturbance in the attacks was not great. The skin over the swellings was purplish in colour. In one of these attacks a portion of the swelling was excised; a large quantity of blood-stained serum escaped, and the tissue removed was pale and oedematous with dark haemorrhagic streaks. Microscopical examination shewed clots undergoing rapid organisation. The patient recovered from the various attacks, with slight weakness and atrophy of the muscles affected. The tendency to the attacks remained.

*Prognosis.*—The disease, which is generally fatal, varies in its duration; one patient died in ten days, and another lived for more than six months after the first symptoms.

**Polymyositis in Association with Erythema Multiforme and Urticaria.**—In erythema nodosum it is not uncommon to find the

underlying muscles hard and tender to pressure; but as the erythema nodosum clears up, the tenderness of the muscles passes off; in some reported cases, however, the affection of the muscles is by no means so transient. The cause of this form of myositis is obscure, cultures made from the muscles having given negative results. But the association with erythema nodosum and urticaria would indicate that the poison is probably of intestinal origin.

*Symptoms.*—The disease commonly affects the lower extremities, and in the slighter form comes on suddenly with severe urticaria of the skin and swelling of the muscles. The swollen muscles are tender, and any movement, either active or passive, is acutely painful. In the severer form the lower extremities are considerably swollen, and small indurated areas can be felt in the muscles. As a rule the disturbance of temperature is not great. Occasionally the joints also are affected.

*Course and Prognosis.*—The disease tends to rapid recovery; the acute symptoms pass off in a week, but some tenderness of the muscles may persist for a time. This form is prone to relapse. Muscular atrophy is said to occur as a result of this affection.

(b) **Neuro-Myositis.**—This name was given by Senator to a form of myositis in which the nerves were implicated as well as the muscles. Neuro-myositis is distinguished from a polymyositis by the presence of sensory as well as motor disturbances. The clinical symptoms may be divided into (a) those due to affection of the nerves, and (b) those due to affection of the muscles. The nervous symptoms are muscular paralysis, tenderness of the nerve-trunks, loss of tendon-reflexes, paræsthesia, and loss of all forms of sensation. There may also be ataxia; and vaso-motor disturbance of the extremities and local sweating may appear. Atrophy of the muscles occurs at a later stage. The muscular symptoms are very variable in extent; in some cases there is only tenderness of the muscles on pressure, whereas in others there is swelling of the muscles. Movements, however, always give rise to pain.

A somewhat different conception of the disease is adopted by Sir W. Gowers. According to him, the disease usually affects one limb, which is tender, and the pain is especially caused by muscular contraction. The joints and nerve-trunks may be affected, but are less tender than the muscles. The disease occurs in patients after the second half of life and usually follows "rheumatism." The symptoms indicate an interstitial inflammation of the muscles, affecting the tissue in which the afferent nerves begin. The arm while at rest gives rise to but little pain, but the sudden contraction of the muscles is acutely painful. If, however, the arm be moved slowly and steadily, a wide range of movement is possible, and it is only the occurrence of a more sudden movement that causes pain. This fear of pain usually results in the arm being held in a fixed position. The muscles are tender to the touch, and somewhat wasted and flabby. The disease is of long duration, and it is only by patient treatment that improvement slowly takes place.

(c) **Tuberculous Myositis.**—Tuberculosis may occur in muscles as

the result of direct extension from neighbouring infected tissue, or may commence in the muscle itself; the former condition is of but little clinical importance, and the latter condition is very rare, and supervenes on tuberculous disease elsewhere. The disease is of gradual onset, giving rise to some pain and localised swelling in a muscle. The swelling is only tender on marked pressure and is often quite painless. The functions of the muscles remain good. The disease runs a chronic course, and the local conditions give rise to but little trouble, unless an abscess forms.

(*d*) **Syphilitic Myositis.**—Two forms are described—(*a*) diffuse syphilitic myositis; (*β*) gumma of muscle.

(*a*) *Diffuse Syphilitic Myositis.*—According to Lewin this form of myositis generally appears between the second and ninth month after infection, 50 per cent of his collected cases occurring during the first year after infection. Lorenz, however, stated that the majority of cases fall between the first and fourth year after infection, and that it may appear as late as the fifteenth year. The muscle most likely to be affected is, according to Neumann, the biceps, this muscle being affected eight times in 11 cases. Lorenz, on the other hand, found that the masseters and temporal muscles are most commonly implicated, and then mentions the sterno-mastoid, the pectorals, deltoid, biceps, and calf muscles.

**Morbid Anatomy.**—Diffuse syphilitic myositis is in its first stage attended by swelling of the muscle, with deposit of a plastic material between the muscular fibres. In the later stages this material undergoes fibrous change, and the muscle-fibres atrophy. The microscopical appearances described are: dilatation of the vessels and thickening of their walls, exudation of granular cells, and at the same time proliferation of the muscle-nuclei, the cells lying in part between the primitive bundles, and in part between the individual muscle-fibres. In the later stages of the disease there is an increase of interstitial connective tissue and the individual muscle-fibres become separated from one another. Lastly, the muscular fibres become opaque and their contents granular, and their striation disappears. Some fibres, however, undergo simple atrophy, and then the striation is preserved even in the smallest fibres.

**Symptoms.**—The disease is gradual in its onset, starting with pain (generally worse at night) in one or more muscles, and attended with redness of the skin and some tenderness on pressure. There is diminished power in the muscles, and movement, whether active or passive, greatly increases the pain. The temperature is often slightly raised. The muscle feels hard and brawny, and there may be a contracted position of the limbs, which varies according to the muscle affected. The condition may be limited to one muscle, or may, after a few days or weeks, spread to other muscles. Recovery is slow, and is often attended by considerable atrophy of the muscle or muscles affected. Many cases, however, recover completely.

( $\beta$ ) *Gumma of Muscle*.—This condition, according to Lewin, occurs at a later period after the primary infection than the foregoing change, in one case as long as thirty years.

*Morbid Anatomy*.—The gummas of recent formation are not so sharply defined from the muscular tissue as those of longer standing. In the muscular tissue immediately around the gumma, the muscle-fibres are separated from one another by small-celled infiltration, and present a variable degree of atrophy. The fibres retain for the most part their transverse striation and nuclei. In the older cases dense fibrous bands lie between the muscle-fibres.

*Symptoms*.—The affection is attended by very little pain, and the patient at first notices a hard swelling in the muscle, which is not tender on pressure, though some pain may be caused in the muscle when it is put into action. Out of 69 cases of muscle gumma collected by Lorenz the sterno-mastoid was affected in 26. In order of frequency other muscles were affected as follows: the quadriceps extensor, the muscles of the calf, the biceps, the forearm, the masseters, and the pectorals. The disease is sometimes symmetrical, being so in 3 out of 7 cases collected by Eger. The central portion of the muscles is that which is most commonly affected.

The presence of the tumour may give rise to very little disturbance of function in the muscles. The course of the disease depends largely on the time taken in the formation of the gumma. When growth is rapid and is met by antisyphilitic remedies recovery soon follows. On the other hand a tumour which forms slowly, disappears slowly, and may leave an indurated mass in the muscle. The tumour seen in the sterno-mastoid muscle of infants is by some regarded as a gumma, and probably correctly so in a small proportion of the cases. In these cases the tumour is not noticed at birth, but has been seen to appear in the first few weeks of life.

*Treatment*.—The treatment of both these conditions consists in mercurial inunction and the administration of iodides. During the more acute stages of the disease the limbs should be kept at rest. In the later stages massage and passive movement may be used.

( $\epsilon$ ) *Myositis due to Trichinella spiralis*.—(See Vol. II Part II. p. 908.)

**B. SECONDARY AFFECTIONS OF MUSCLES.**—( $\alpha$ ) *Myositis due to the Specific Fevers*.—The changes occurring in muscles during the course of the specific fevers should be regarded as degenerative rather than as inflammatory; these changes have been especially found in the course of enteric fever, and they give rise to a dull, pale, fish-like appearance of the muscle. On microscopical examination the fibres are seen to be swollen and hyaline, the transverse striation having disappeared; this process usually affects some of the fibres only, the others retaining their striation. When suppuration takes place in the muscle, the abscesses have been found to contain streptococci, staphylococci, and other micro-



organisms; they are therefore due to infection, and belong to the following class:—

(b) **Infective Myositis.**—This may be due to infection in pyaemia, puerperal conditions, infective endocarditis, glanders, actinomycosis, or to an infected wound or boil. The disease is often attended with rigors, the local muscular symptoms being masked by the general symptoms. The disease frequently ends fatally.

*Morbid Anatomy.*—The muscles have a dirty-red colour, and on pressure a greyish-red fluid exudes. Microscopical examination shews loss of the transverse striation and increase of the inter-muscular cells and, in suitably stained specimens, micro-organisms in the muscular tissue. The occurrence of definite abscesses in the muscle would seem to depend on the length of time that the disease has existed; in some cases in which the general infection has been very acute no abscesses have been found in the muscles, whereas in more prolonged cases numerous abscesses occur.

Bacteriological examination of the muscle and of the pus shews the presence of streptococci; these, however, are not always present in great numbers in the muscle; and such a case, in which the micro-organism escaped detection in the muscle, and in which the source of infection was not obvious (for example, the ear), might well pass for a case of polymyositis so long as suppuration did not occur.

*Diagnosis.*—The occurrence of rigors and the affection of the joints, together with the difference in the character of the skin affection, should distinguish it from polymyositis.

Myositis due to gonorrhoeal infection is dealt with in the article on Gonorrhoeal Rheumatism (Vol. III. p. 48).

**MYOSITIS OSSIFICANS PROGRESSIVA.**—Although this condition is usually known as myositis ossificans, it seems well to add the epithet “progressiva,” so that the disease may be distinguished from those cases in which there is local ossification of a single muscle, and from those cases in which multiple exostoses extend into the muscles; the latter cases are sometimes hereditary. The description of myositis ossificans progressiva from a clinical aspect is not difficult, for the onset and course of the disease are strikingly similar in all cases.

*Historical.*—The earliest case was reported in 1740 by Freke, in a boy fourteen years old, who began to have swellings on the back three years previously; these swellings continued to grow. “They arise from all the vertebrae of the neck and reach to the sacrum; they likewise arise from every rib of the body, and joining together in all parts of his back as the ramifications of coral do, they make as it were a fixed bony pair of bodice.” A far more complete account is furnished by Robert, Bishop of Cork, and the Rev. Dean Copping of one William Clarke “whose name I shall endeavour to transmit to future ages.” The patient, who began to become stiff when eighteen years old, died when sixty-one. At the time of his death the only bones he could move were the wrist

of his right hand and the bones of his knees. For many years before his death he could not alter his position in the least. Dr. Barry of Cork prepared his skeleton, and gave the following account of it: "Not one bone in his body has the natural form, for all his joints are immovable and ossified. And such a luxuriant disposition had all the humours of his body to turn into bone, that many little branches of



FIG. 1.—Skeleton of myositis ossificans progressiva (Barry)

bone, like coral, spring from the joints and several parts of the body. The whole spine is ossified and one entire arch of bone there is from the occiput down to the os sacrum, out of which arises a very protuberant bone, which serves as a fine handle to the skeleton. A sharp horn like a cock's spur grew out of his heel every year. It is as difficult to give a particular and exact description of this curious memento mori as of Calypso's Grotto."

In 1869 Münchmeyer adopted the name myositis ossificans progressiva, and gave a most accurate description of the disease, based on

12 collected cases, 9 males and 3 females. In 1879 Helferich noted the occurrence of an ankylosis of the phalanges of the thumb and a lack of one phalanx of the great toe. Since that time the literature has been carefully and fully reviewed by Pinter (1884), Pincus (1896), Roth (1898), and De Witt (1900); but some of the cases recorded can hardly be regarded either clinically or pathologically as myositis ossificans progressiva, as they are simply instances of local ossification of muscles.

**Morbid Anatomy.**—Our knowledge is based on a few necropsies, and on the examination of excised pieces of muscles. In the early stage of the disease the appearances are those of acute myositis; the second stage shews increase of the intramuscular connective tissue, with subsequent contraction, giving rise to atrophy of the muscular fibres, and a fibrous condition of the muscles; the third stage is that of ossification of the fibrous tissue formed. In the first stage there is an increase of connective tissue, especially in the neighbourhood of the vessels (Fürstner). The swelling at this period is chiefly formed of young connective tissue, the muscular fibres for the most part being normal. Macroscopically, the affected muscle appears swollen, oedematous, of soft consistency, and a yellowish-red colour. In the second stage the muscular tissue gradually becomes converted into a hard and fibrous tumour, the only remains of normal tissue being a thin membrane, which covers over the surface of the tumour. Lexer found that the central part of such a muscle consisted of a firm fibrous bundle, with radiating bands of fibrous tissue, among which were atrophied muscular fibres. Numerous capillaries pervaded this tissue. In the third stage true bone is formed in the fibrous tissue. Boks examined an excised bony portion microscopically, and found that in certain parts the various stages of the formation of true bone in fibrous tissue could be traced. Fürstner, Lexer, and Boks shewed that ossification started in the connective tissue between the muscular fibres. No primary change has been found in the muscles, but they shew secondary atrophy and fatty degeneration.

**Pathology.**—As to the cause of the disease, nothing is known. It may be described as an “inborn error of metabolism,” or “a luxuriant disposition of the humours of the body to turn into bone.”

By some writers it has been regarded in the nature of a new growth, but neither from the clinical nor pathological standpoint is there sufficient evidence for this conception.

**Sex.**—Males are more frequently affected than females; of the 39 cases collected by Roth, 30 were males and 9 females.

**Age.**—The disease starts in early infancy. Dr. Garrod records a case in which the earliest symptoms were noted at five months.

**Clinical Features.**—The symptoms of the disease are well defined and strikingly similar. The first symptom is usually a local swelling over the back, which is attributed to injury. The swelling, situated in the muscles, is firm in consistency, sometimes painful, and may be accompanied by some fever. There is often more or less oedema round



the swelling, but the skin itself is free. After a few days the swelling tends to go down, leaving merely a hardness in the muscles, which may gradually develop into an actual tumour.

Dr. Garrod, in his description of the condition in a child twenty-one months old, says the swellings were of various sizes and differed in their characters. They were most numerous upon the back, but two were situated on the front of the chest, apparently in the outer part of the pectoral muscle, and there was a single swelling over the occipital bone. The swellings on the back formed round or oval bosses, very firm and elastic, with sharply defined margins; they were attached to the deeper structures, and the skin was freely movable over them. They were not tender, and there was no discoloration of the skin. From the bases of some of the more defined swellings, slender processes could be traced for some distance from the main boss. Swellings of a second kind appeared to be diffuse thickenings of the soft parts, with indefinite outline, and over these the skin was not movable; these thickenings were mainly in the lumbar and sacral regions, and pitted on pressure. A remarkable phenomenon was observed in some of the masses, in that they underwent fission, a single boss becoming converted into two discrete bosses connected by an area of diffuse swelling. Fission might take place more than once in such bosses. The duration of such swellings, from the time of onset to complete disappearance, varied from nineteen to thirty-seven days.

After a few weeks, or months, fresh attacks occur, with further swellings in the muscles; and these again may either subside completely, or leave some residual hardness. The condition in its earliest stage is commonly regarded as muscular rheumatism. The swellings sometimes appear without pain, and without any obvious injury. The recurrence of painful swellings in the muscles is very characteristic of the disease. All the tumours do not form bone; some disappear altogether, whilst in others the muscle becomes atrophied. When once formed, a bony growth never disappears. The bony tumours are at first small and multiple; they gradually enlarge and coalesce, so as to form long bony masses of most irregular and fantastic shapes. At first these masses are independent and free from the bone, but in the progress of growth they become attached to the bone and give rise to a great limitation of movement. The disease gradually affects all parts of the body, leading to complete fixation of the neck, trunk, and limbs, so that the patient is entirely helpless.

The disease commonly begins in the muscles of the neck and back, especially in the *latissimus dorsi*. In 21 out of 38 cases the disease began in the back and neck, in 7 cases in the shoulder, in 4 in the throat, twice in the masseters, twice in the arms, and twice in the lower extremities. The muscles of the back are always affected, and in advanced cases the back is always bent and immovable; the neck too is fixed, and the head bent to the side. The shoulder-blades become fixed to the thorax, so that movements of the arms become impossible, and the patient is

unable to feed himself. Gradually the ossification of the muscles of the back increases, and it is no longer limited to those muscles. The ligamentum nuchae may become ossified and the spinous processes fixed to

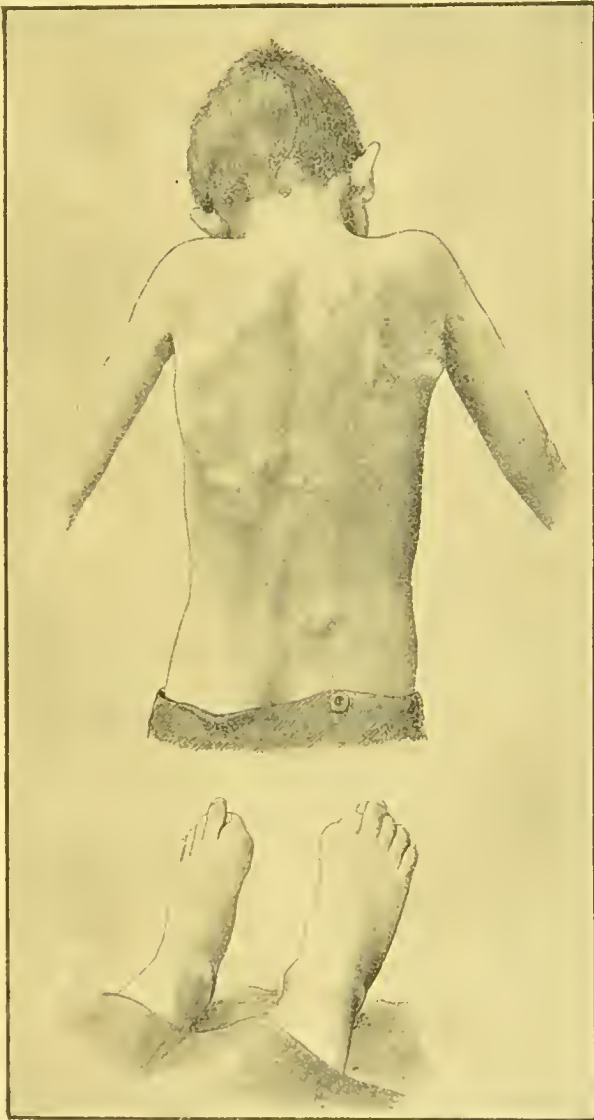


FIG. 2.—Myositis ossificans. Bony nodules on the back, neck, and iliac crest. The feet shew microdactyly (Simpson).

one another. Exostoses appear on the ribs and fix the thorax. After the muscles of the back and shoulder, those of the limbs are attacked, those of the upper extremity being usually implicated earlier than those of the lower. The affection of the masseters and temporal muscles brings about a pitiable condition; the patients cannot eat, and the jaw

is absolutely fixed. Even the ocular muscles have been found to be affected. Certain groups of muscles escape—the muscles of facial expression, the platysma, the tongue, the muscles of deglutition, of the larynx, the diaphragm, the heart, the muscles of the perineum, of the genital apparatus, and the sphincters. The electrical irritability of the muscles is lost when the disease is advanced, but in others the faradic irritability is maintained.

*Microdactyly* is common, and is said to be present in 75 per cent of the cases. A symmetrical deformity of the great toe has been present in several cases; the great toe is shorter than the second toe, and this deformity is due either to the absence of the proximal phalanx or to a synostosis of the shortened phalanges of the toe, which, without an x-ray photograph, may easily be mistaken for the absence of the proximal phalanx (Fig. 2). Ankylosis of the thumb, with shortening and a lack of growth in the thumb and in the little finger of both hands, has been described. Dwarfing of the lower jaw has also been recorded.

**Course.**—The disease, starting in early childhood, is slowly progressive. Pauses occur, in which improvement may be manifested, and exacerbations occur, in which the disease makes rapid progress; the disease is seldom rapid in its development. The periods of exacerbation, with fever and the formation of swellings, last but a few days; the absorption of the swellings takes from two to three months, and often leaves a bony residue. The intervals between the attacks vary from a few weeks to several years. When once formed, the tumours remain unaltered. The disease always advances by acute attacks, never gradually. The patient lives on for years, becoming gradually more and more fixed, and dies of tuberculosis, pyaemia, or some other intercurrent affection.

**Diagnosis.**—When well developed, the disease has such marked features that there is no difficulty in diagnosis. But in its early stages it is commonly mistaken for rheumatism, or regarded as the result of injury. Multiple exostoses may, when extensive, give rise to ossification of some portion of a muscle, but never to the free masses of bone found in myositis ossificans. Multiple exostoses may be hereditary, but there is no evidence of this in myositis ossificans; two remarkable cases of hereditary ankylosis of joints, however, have been recorded (Drinkwater, Walker).

**Treatment.**—No known remedy has any influence in arresting the course of the disease. An exacerbation so often follows an injury, and these patients fall so readily, that it is almost unnecessary to point out the need for great care in these respects. Resection of the jaw has been performed, so that the mouth may be opened; but the removal of a few teeth satisfactorily provides for feeding.

**MYOSITIS FIBROSA.**—Very few cases of this rare disease have been described, and in these there is considerable difference in the clinical features. As in myositis ossificans, there are the two forms: (a) in which

there is a local fibrous condition, produced by injury or infection; of this Biggs has given a good description; (b) in which the condition is general and progressive. The second of these two conditions is described here.

**Morbid Anatomy.**—The muscles are firm and hard, and when cut are found to consist of a tissue which grates under the knife and appears hard and white on section. In less affected portions the tissue appears spotty, from the remains of muscular tissue which form reddish-yellow points on a white background.

*Microscopical examination* shews an increase of the interstitial tissue between the muscle-fibres, which have in part undergone granular degeneration, in part simple atrophy. The most severely affected portions of muscle are composed entirely of tendinous tissue.

**Pathology.**—The cause of the disease is obscure; injury, syphilis, rheumatism do not appear to play any part. The clinical features closely resemble those seen in myositis ossificans, and in one reported case the great toes were shorter than the second toes. The increase of tendinous tissue in the muscles would seem to suggest that the tendon tissue has proliferated; on the other hand, it is possible that the tendon tissue is only relatively increased, owing to the extensive shortening of the muscles.

**Clinical Features.**—The disease starts as a subacute inflammation of muscles and produces a chronic myositis, which affects successively various groups of muscles and slowly advances. The lower extremities are usually first attacked, but in the case described by Janicke the disease began in the sterno-mastoid muscle, spread to the neck, back, and intercostal muscles, and later to the abdominal muscles.

The disease would seem to start in early life. In a case which I published, a boy, aged six years, had been well till the age of nine months; the mother then noticed that the back was growing out and the legs were drawn up. The condition slowly progressed, and the child became more bent up. There was no acute onset, and the child did not seem to have any pain; this is a point of interest, as in some of the reported cases pain appears to have been a prominent feature. The child could sit in bed with the legs flexed, the back curved, and the head flexed on the chest, and the face turned towards the left, owing to contraction of the right sterno-mastoid. The spine was fixed in a curved position and could not be straightened. The abdominal muscles were extremely hard and contracted. The arms were fixed, so that they could not be extended or adducted (Fig. 3). Any attempt to move the boy resulted in his moving as a whole. He was rigidly fixed in a flexed position and was unable to move. There was no evidence of any affection of the joints. The only osseous deformity present was that the great toe was shorter than the second, third, and fourth toes.

**Course and Prognosis.**—The disease would seem to run a steadily progressive course, but the cases reported by Janicke, Gies, and Kreiss recovered.



**Diagnosis.**—The diagnosis must always present considerable difficulty. The clinical resemblance to myositis ossificans is sometimes very close; and it is only the complete absence of any evidence of bony formation within the muscles that justifies the diagnosis of myositis fibrosa.

To the later stages of myopathy, again, the disease bears considerable resemblance, but in myopathy the wasting of muscle, either general or in localised groups, is very characteristic. To the chronic arthritis of children the disease bears some resemblance, owing to the flexed condition of the limbs, but the implication of the joints, and the other glandular and visceral symptoms, serve to distinguish these two conditions.

In cerebral diplegia, again, there may be such marked rigidity of the



FIG. 3.—Child with myositis fibrosa.

limbs and contraction of muscles that the patient is in an almost immovable condition. The presence of well-marked signs of cerebral and spinal disease would serve to distinguish such cases from myositis fibrosa.

**Treatment.**—In the later stages of the disease, when the place of the muscular tissue is taken by fibrous or tendinous tissue, little can be done in the way of treatment. In the earlier stages, however, massage and passive movements might be beneficial, and might lead to complete arrest of the disease. Both Gies and Kreiss report cases which recovered under treatment with massage and electricity. Hot-air and other baths should be given a trial; iodide of potassium and mercury might be used in suitable cases. Injection of thiosinamine (fibrolysin) would seem to

have the power of stimulating absorption of fibrous tissue, and might be tried. It has been employed in other fibrous conditions of muscles (pseudo-hypertrophic paralysis), but without success, and is not without risk.

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F. E. B.

#### AMYOTONIA CONGENITA

SYNONYMS.—*Myatonia Congenita*; *Oppenheim's Disease*.

By JAMES COLLIER, M.D., F.R.C.P.

**Definition.**—A malady of early childhood, usually congenital but never familial, characterised by extreme flaccidity, smallness and lowering of

the faradic excitability of the skeletal muscles which are not actually paralysed, by loss of the deep reflexes, and by contractures in the regions affected. The distribution is always symmetrical. The lower extremities are the most often and the most severely affected, the face being exempt. All cases have shewn a tendency to gradual improvement.

**History.**—Oppenheim (17) in 1900 described a case with such peculiar and striking symptoms and so unlike any other disease of infancy in its clinical manifestations as to warrant the separation of a new clinical entity which he termed “Myatonia Congenita.” In 1903 Dr. Batten described 3 cases under the name “Myopathy of an Infantile Type.” In 1904 Oppenheim (18) and Schüller described further cases, and since this time many other cases have been reported which have been in strict conformity with Oppenheim’s type. In this country 5 cases were published in 1907 by Drs. Carey Coombs, C. E. Beevor, and by Collier and Wilson, and since then fresh observations have been recorded (Wynter, Collier and Holmes, Theodore Thompson). Pathological investigations have been made by Spiller, Bandouin, Bing, Variot and Devillers, and by Collier and Gordon Holmes.

**Etiology.**—Little is known of the causal factors of the disease. The sexes seem to be equally affected. A high majority of the cases have been congenital, but in a few examples the malady has commenced in the first year of life in a previously healthy child, apparently as the direct result of acute bronchitis or of diarrhoea. Until quite recently no case had been reported with either a familial or an hereditary tendency, or in which any association of this disease with myopathy had occurred, points which have been held to be highly characteristic of amyotonia. But in 1909 Sylvestri recorded 2 congenital cases in children of the same mother. A maternal aunt suffered with the Landouzy-Dejerine type of myopathy. The elder of these children, after progressive improvement from the time of birth to the age of sixteen years, developed Erb’s juvenile type of myopathy with pseudo-hypertrophy of some of the muscles of the pectoral girdle. The familial cases reported by Sorgente as examples of amyotonia were certainly not instances of the disease. Morbid conditions in the parents and maternal ill-health during pregnancy have been conspicuous by their absence. In every case birth has occurred at full term, and the children have been of good weight, and have seemed in other respects physically healthy.

**Morbid Anatomy and Pathology.**—The skeletal muscles of the affected regions shew a very striking departure from the normal, the change varying in degree according to the extent to which the individual muscles are involved. Macroscopically the muscles are small, somewhat yellow in colour, and are with difficulty separated from the surrounding tissue. When cut across, the prismatic muscle-bundles are more conspicuous than in the normal muscle, and there is often a considerable amount of fat separating the muscle-bundles. The amount of this deposit of fat seems to increase with the age of the patient; it was inconspicuous in the case of a patient aged two years, and was very well



marked in a second case examined at the age of seven years. It never reaches the degree met with in pseudo-hypertrophic paralysis.

The characteristic microscopical features of the affected muscles are (1) the minute size of the majority of the muscle-fibres which do not exceed  $12\mu$  in diameter, and many of which are not more than  $7\mu$  in diameter, and (2) scattered among these minute fibres are a few very large fibres reaching  $140\mu$  in diameter, and larger than any fibres met with in normal muscle. The transverse striation of both large and small fibres is well marked, and the fibrillar areas of the large fibres are well shewn. Many of the small fibres shew scarcely more nuclei than may be found in normal adult fibres, but in some of them there is a great proliferation of the sarcolemmal nuclei which may reach such a degree as to conceal the substance of the fibre; this increase seems to be more marked in the cases of longer duration. No degenerative or regressive changes have been found in the small fibres. The greatly enlarged fibres only rarely form bundles of themselves, but they are placed in or between the bundles of small fibres. Apart from their size and their unnaturally cylindrical shape, most of these giant fibres have a normal structure and their nuclei are only found under the sarcolemmal sheath. In a certain number of them, however, unmistakable regressive changes occur, such as the presence of central nuclei, central vacuolation, and invasion of the myoplasm by the sarcoplasm and sarcoplasmic nuclei, whilst in longitudinal sections some of these giant fibres can be seen in the process of splitting up lengthwise into apparently well-formed fibres of small calibre, provided with a normal sarcolemmal sheath and nuclei. This occurrence probably explains why the giant fibres are much less numerous in cases of long duration. There is great increase of the connective tissue of the affected muscles and a notable determination of loose fat between the muscle-bundles.

The ventral nerve-roots of the affected regions shew conspicuous changes when compared with the corresponding dorsal roots, for not only are the fibres much reduced in number, but they are individually slender and poorly myelinated. The only changes found in the central nervous system are confined to the ventral horns of the spinal cord, where the large cells of the motor type are much reduced in number. In one of my cases there appeared to be scarcely a third of the normal number of cells present, and these were individually smaller and more irregular in shape than are normal cells. In a case reported by Spiller the thyroid and the thymus glands were fibrosed.

Oppenheim was the first to suggest that the nature of the malady was essentially an arrest of development of the muscle-fibres, and this view seems in accord with some of the clinical features of the congenital cases, and especially with the tendency of many of the cases to improve progressively. The post-natal onset of the malady in some cases is difficult to explain in this light; and, moreover, it has been shewn by Dr. Gordon Holmes and myself that the affected muscle-fibres in amyotonia do not present the appearance of undeveloped fibres, for the central

portions of the small fibres are well differentiated and they possess well-developed sarcolemmal sheaths. Baudouin concluded that the changes in the muscles were intense regressive lesions of the same nature as are met with in the myopathies, and the pathological investigation which Dr. Gordon Holmes and I have made in 2 cases lead us to the same conclusion. We cannot, however, agree with Baudouin that the muscular changes depend upon changes in the lower motor neurons, since the changes found in the latter may be secondary to the muscular affection, and since identical changes have been found in the ventral horn cells in some cases of myopathy. If we accept the pathological conception that amyotonia is dependent upon muscular regression there is great difficulty



FIG. 4.—Amyotonia congenita. Shews the difficulty of holding up the head, the extreme external rotation at the hips, the pad-like feet, and the dorsiflexion of the ankles.

in accounting for the tendency to progressive amelioration that most of the recorded cases have shewn, and for the present this clinical feature of the disease must remain at variance with our pathological knowledge. Cattaneo has suggested that a disorder of internal secretion is primarily responsible for amyotonia, but there is little or no evidence upon his side.

**Symptoms.**—The extreme flaccidity of the muscles of the regions affected is usually noticeable from the time of birth, and is most intense at this time, slowly improving subsequently. The muscles are small and weak, and cannot be felt as separate from the skin and subcutaneous tissue, but there is not any local muscular wasting, nor is there any complete paralysis of voluntary movement in any individual muscle, though the lower limbs are always too feeble to support the body, and in many cases the limbs cannot be raised against the action of gravity. The

great relaxation of the muscles and of the ligaments allows the most fantastic positions of the limbs to be assumed without pain. Hyper-extension of the joints and double-jointedness are common, and when the upper extremity is affected, if the forearm be held and shaken by the observer, the fingers move like the tails of a many-tailed whip. Sometimes many of the joints are flail-like. A characteristic position of rest is often assumed by the feet, namely, extreme hyper-extension of the ankle-joint, so that the whole length of the dorsum of the foot is in contact with the front of the tibia. When the trunk is affected the child sits bunched up with an obvious kyphosis which disappears completely when he is raised by the shoulders.

The distribution of the amyotonia is always symmetrical. The legs have been affected in all the cases; the trunk is usually involved; the upper extremities are often affected, but the face rarely. The diaphragm usually escapes even when the trunk is severely implicated. The ocular muscles, the orbicularis oris, and the muscles of mastication and deglutition are never affected. Where all four extremities are involved, the upper may be more affected than the lower, and the trunk may escape altogether. Contractures are often present in the lower extremities, usually slight flexor contracture of the hip and knee, more rarely contractures of the calf muscles are found with consequent deformity of the foot.

The faradic excitability of the affected muscles is lowered, and where the amyotonia is present in high degree they only respond to the strongest stimuli, whereas the galvanic excitability is normal. Though there is no demonstrable loss of pain-sensibility, nor of any other form of sensibility, yet the strongest faradic stimulation of the affected region is often borne without complaint, and this is a highly characteristic feature of the disease. The sphincters are never affected.

The superficial reflexes are normal. The deep reflexes are invariably absent in the affected regions, but in cases in which great recovery has occurred they appear and remain permanently.

Intelligence is normal, and the special senses and cranial nerves are not affected. The bodily development is good, and the growth of the bones in the affected regions seems to be normal.

**Course.**—The course of the disease is one of very slow improvement, and this improvement may be materially hastened by appropriate treatment. In limbs that are not severely affected recovery may be rapid, as in a case under my care in which the upper extremities recovered completely with return of the deep reflexes after three months treatment. No increase of the symptoms has been observed in any case. Whilst many of the cases have improved markedly, yet in no recorded instance has complete recovery been attained.

**Diagnosis.**—The diagnosis of the disease does not present any difficulty, for the clinical aspect is entirely unlike that of any hitherto described disease of childhood. The presence of the symptoms soon after birth, the extreme muscular flaccidity, the absence of the deep reflexes,

the peculiarity of the electrical excitability, and the absence of complete paralysis and of any loss of sensibility will at once serve to distinguish amyotonia from those diseases of childhood to which it may bear a slight and superficial resemblance, namely, rickety weakness, obstetrical palsy, infantile paralysis, and diphtherial palsy. The distinction of this malady from the myopathies, and especially from simple myopathy, depends upon the following points:—Amyotonia is, in the majority of cases, congenital, whilst in a small minority of cases it appears suddenly and in a fully-developed form after certain acute diseases. The local weakness and wasting of an individual muscle or group of muscles, which is so characteristic of all forms of myopathy, are not met with in amyotonia. Affection of the periphery of the limbs and especially of the intrinsic muscles of the hand, which is the invariable rule in amyotonia, is of the greatest rarity in any form of myopathy. Amyotonia never spreads to regions previously unaffected, whereas a slow spread of the affection from muscle to muscle is characteristic of all forms of myopathy. The deep reflexes are absent from the first in amyotonia, whereas in myopathy they are present at first and slowly diminish, and are lost as the affection of the muscles concerned increases. The deep reflexes may appear in amyotonia when improvement occurs, and having appeared remain permanently. In myopathy the deep reflexes never reappear after disappearance. Lastly, a majority of the recorded cases of amyotonia have shewn a tendency to progressive improvement.

**Treatment.**—The natural tendency of this disease to improve slowly may be much assisted and this result hastened by the regular and long-continued use of massage and of passive movements, the application of which can be easily learnt by the mother or by the nurse of the child. The child should be induced to move the weak limbs as much as possible and in such positions as they are least encumbered by the action of gravity. The use of mechanical supports of any kind is absolutely to be deprecated. Where contractures are severe, tenotomy and tarsectomy have been successfully employed. The medicinal remedies that have proved of service are general tonics, iron, strychnine, and cod-liver oil.

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J. C.

## MYOTONIA CONGENITA

SYNONYM.—*Thomsen's Disease.*

By W. HALE WHITE, M.D., F.R.C.P.

**Definition.**—Thomsen's disease is a malady the chief feature of which is that upon the execution of any voluntary movement the muscles brought into play remain contracted for some seconds.

**History.**—It is usually said that Sir Charles Bell first described this disorder; but he did not give it a name, and I think that any one reading his description will agree that it is extremely doubtful if his cases were really examples of Thomsen's disease. Two cases were referred to by Benedikt in 1864; but it was the publication, in 1876, by Thomsen, a Danish physician, of a description of the disease as it existed in himself that first directed attention to it. Since then several cases have been published; but the disorder is excessively rare. In 1890, when I collected all the recorded cases, shewed one at the Medical Society, and published an account of it, only one case had been shewn at the Medical Societies of Great Britain or mentioned in our medical journals; namely, that exhibited by Dr. T. Buzzard at the Neurological Society in 1887. The disease appears to be equally rare in all countries, but not limited to any.

**Etiology.**—No cause has been discovered. One or two cases have been set down to fright; but in the great majority there is no evidence of this.

**Heredity.**—In nearly all the recorded cases the disorder has existed in several relatives of the patient—generally in one of the parents, and in the patient's brothers, sisters, and children. This is so marked a feature that it must be regarded as one of the characteristics of the disease. Several of Thomsen's relatives were affected with it, and my patient's father and sister and two of his father's cousins had suffered from it.

Some authors have been inclined to lay stress upon the presence of other neuroses in the same family. Many of Thomsen's ancestors suffered from mental weakness; nevertheless, as it is so often expressly stated

that there was no neurotic history, I do not think that a family history of neuroses has much bearing on the matter. The patient himself is rarely of neurotic habit.

*Age.*—When the patients first come under observation they are usually about twenty years old or younger. Generally they say either that they have had the disease as long as they can remember, or that it came on in childhood, when they first noticed that they could not take part in games because of the stiffness of the muscles.

*Sex.*—It is much commoner in males than in females. Among 102 cases collected from literature by Hans Koch 91 were men and 11 women.

*Histology.*—There is only one published account of a necropsy upon a case of this disease, that recorded by Dejerine and Sottas. Their patient, a man aged thirty-seven, died of acute nephritis. They could not by the most careful examination find anything abnormal in the brain, spinal cord, or peripheral nerves. Their examination of the muscles confirms in every particular the description given by Erb, Neuronow, myself, and others, all of whom took a piece from the affected muscles during life. My patient willingly consented, and under chloroform a small piece was cut out of the flexors of the left forearm. The most important abnormality of the muscle in Thomsen's disease is the great width of the muscular fibres. Those of my patient were from  $\frac{1}{2} \frac{1}{50}$  to  $\frac{1}{5} \frac{1}{60}$  of an inch wide. The normal width of the fibres of the voluntary muscles of the limbs is, according to Quain, from  $\frac{1}{4} \frac{1}{60}$  to  $\frac{1}{7} \frac{1}{50}$  of an inch; and I controlled the examination by some normal fibres from the flexors of an adult forearm, and found them to vary between  $\frac{1}{3} \frac{1}{50}$  and  $\frac{1}{2} \frac{1}{60}$  of an inch in width.

Thus we see that in Thomsen's disease the fibres are quite double the width of those in the normal state: indeed, cases have been described in which they were four times as wide. The transverse striation is always very feebly marked, the border of the fibre is slightly and irregularly curved, and the nuclei of the sarcolemma are increased in number. Some observers have described an increase of the connective tissue between the fibres. If present at all, it is very slight.

In the cases in which atrophy supervenes the fibres degenerate.

*Pathology.*—The occurrence of the disease in several members of the same family, and the fact that it is nearly always first detected in childhood, shew that it is congenital; and it would appear that each individual affected is from his birth faultily constructed, so that some of his muscular fibres all through his life grow abnormally, and in consequence of this abnormal growth contract in an abnormal manner. This is more in

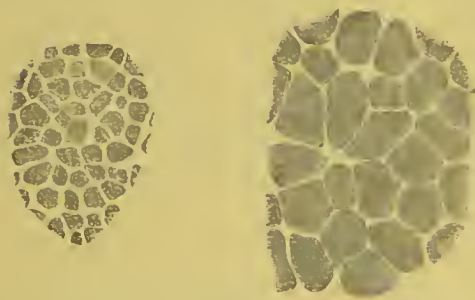


FIG. 5.—Transverse sections of muscle from flexor muscles of a normal person and from a patient with Thomsen's disease for comparison.  $\times 52$ .

harmony with what we know of other diseases than to believe, as Dejerine and Sottas apparently do, that the abnormal contraction of the muscle leads to its abnormal growth. All who have written on the subject agree that it is a disease solely of the muscular system (*vide* also p. 57).

In any discussion on the pathology of the disease, it must always be borne in mind that the peculiar contractions are exactly the same as those which may be induced in animals which have been poisoned by veratria; as may be readily seen by comparing the curves I obtained with those in a textbook of physiology. Drs. Ringer and Sainsbury found that if phosphate of sodium be given to an animal and the sciatic nerve then stimulated, contractions like those of Thomsen's disease are produced; and this even if curare had been previously injected. Hence it appears that the Thomsen-like contractions are due to the action of phosphate of sodium on the muscular fibres themselves, and this experiment and that of giving veratria strongly support the view that Thomsen's disease is a malady of the contractile tissue of muscle.

**Symptoms.**—*Peculiarity of Movement.*—This only occurs in voluntary movements, and consists in the fact that the contraction of the muscle which the patient wills to move is slower than normal, and that, because it relaxes gradually and very slowly, it remains for some seconds more or less contracted; this contraction is so strong that the antagonistic muscles cannot overcome it. If a certain voluntary movement is repeated several times the patient begins to execute each movement before the preceding contraction had completely relaxed, and his difficulty as regards the stiffness gradually becomes less and less in each movement. Walking is very commonly affected; for example, if the patient is standing still and sets out to walk, he puts forward one leg rather slowly, it then remains stiff for a few seconds; the next time it is moved the stiffness is of shorter duration, and he soon walks quite comfortably even for miles; but if he trip against a stone, and thus brings into play some new muscular combination, the muscles newly engaged become stiff, and he may fall down. Flexion of the fingers usually illustrates the peculiarity of the disease very well; it is obvious that the flexor muscles contract more slowly than normal; they appear to remain completely contracted for from one to three seconds, and then they are not at once completely relaxed, for if the patient is told to unclothe the hand as quickly as possible it is often between seven and ten seconds before the extensors completely overcome the flexors; as they do so, first the metacarpo-phalangeal joints become slowly extended, then the middle phalangeal, and finally the terminal phalangeal joints. If flexion be repeated as rapidly as possible the second contraction obviously occurs more rapidly than the first, the third more rapidly than the second; and after about half a dozen contractions the action appears quite normal; yet even then myographic tracings shew that many contractions take place before they become quite regular. The difficulty is the same whatever muscles are affected, and different patients find different movements particularly difficult. Thus the patient, from whom I took tracings, being a carpenter, finds it



difficult to saw, for he cannot start easily, and, when his sawing has become even and free, if he stop to rest the difficulty reappears directly he begins again. He cannot turn his head, nor extend his thighs, nor put out his tongue, nor contract his facial muscles properly. If he is told to open and shut his mouth, it is some few seconds before the masseters and internal pterygoids can overcome the contraction of the depressors of the jaw; but after two or three movements the opening and closing of the mouth become easy. His father finds going up and down stairs particularly difficult. Other patients have noticed the difficulty in dancing and drilling; indeed, the difficulty of which the patient chiefly complains is almost always connected with some movement of the extremities. Occasionally the stiffness is much more marked during the second movement than during the first. These peculiar contractions do not appear to be affected by cold, by direction of the attention to them, by mental excitement, by time of day, by alcohol, by meals, or by temperature; but sometimes, when the patient is fatigued, the peculiarity is especially prominent.

Such a defect in the acts of swallowing, respiration, micturition, defecation, and parturition has never been recorded; but with these exceptions the stiffness may be observed in any movement executed by voluntary muscles. The muscles of the arms and legs are most commonly implicated; the legs, perhaps, a little oftener than the arms. The muscles of the trunk, as shewn in stooping, and those of the head and neck, are often affected; so also are those of the face and of mastication. Some of the rarest muscles to be implicated are those of deglutition, the ocular muscles—affection of which gives rise to squint and diplopia—and the laryngeal muscles. The interossei often escape; my patient can write very well although his long flexors are badly affected. The superficial and deep reflexes are normal. Usually the grasp, as tested with the dynamometer, is, if anything, below the normal standard; this is especially noteworthy, as in these patients the muscles are usually bulky. But several cases have now been recorded (Curschmann; Mannel, E.; Meara, F. S.; Berg, H.) in which the affected muscles have ultimately slowly atrophied, but even after considerable atrophy the characteristic contraction and electrical reactions remain. The term *Myotonia atrophica* may be applied to these cases (*vide* p. 42). In *myotonia congenita* there are no sensory disturbances, and the optic discs are healthy. Sometimes in mild cases in which the peculiar motor symptoms are slight and not many muscles are affected, the characteristic contraction may not always be noticeable; then it is said to be most evident in cold weather. The milder the case, the less likely that many members of the family will be affected. Occasionally one member only is apparently affected, but it is rarely possible to examine all the members of a family, and some who had the disease may have died.

*Electrical Reactions.*—These, which are characteristic of the disease, have been collectively named by Erb the “myotonic reaction.” They are as follows: (i.) The motor nerves do not shew any increase of irritability

to mechanical stimuli; (ii.) To the faradic current the motor nerves are quantitatively normal, but if the current be strong the contraction produced on closing the circuit lasts much longer than it does in health; (iii.) To the galvanic current the motor nerves are quantitatively normal; but here also if the current be strong the contraction lasts longer than in health; (iv.) Mechanical stimuli applied to the muscles, as by hitting them, induce contractions more easily than in health; these contractions often last from five to thirty seconds; (v.) The faradic current applied directly to the muscles, if strong, sets up a contraction which lasts from five to thirty seconds; (vi.) When the galvanic current is applied directly to the muscle, K.C.C. and A.C.C. are equally easy to obtain; whereas in health, as is well known, K.C.C. is more readily elicited than A.C.C. In Thomsen's disease even with weak currents the contraction lasts longer than in health; with strong currents it lasts some seconds and relaxes very slowly. With the stable application well-formed wave-like contractions are seen to proceed slowly from the cathode to the anode.

It is quite exceptional for all the points of Erb's "myotonic reaction" to be observed in the same case. Many observers cannot obtain the wave-like contractions he describes as following the stable application of the galvanic current. On the other hand, I was easily able, by rolling the ulnar nerve of my patient under my fingers, to make the muscles supplied by it contract; although I found by repeated observation that in healthy persons this is not easy to do. The contraction and relaxation were both prolonged, but the patient's muscles did not contract when hit.

*Myographic Tracings.*—Various observers have taken myographic tracings of the movements; my tracings shew in detail the peculiarities of the muscular contraction; for instance, a tracing was taken of the contraction of the flexors of the forearm when the patient opened and shut his hand as fast as he could. The first contraction was very slow, and the muscles took four seconds to reach their maximum contraction. This remained for fully a second, and then relaxation began and was very slow; but the second contraction started 6·15 seconds after the beginning of the first, and therefore well before relaxation was complete. Like the first, it was slow and remained at its maximum a short time, but from the beginning of the second contraction to the beginning of the third was only 4·1 seconds: the second was not so powerful as the first. The interval between the subsequent contractions gradually became shorter and their intensity feebler and feebler until the ninth contraction, when the amplitude became greater; and from then to the twenty-third the interval between the contractions became gradually less, and for the most part the amplitude increased. After this the contractions were regular, frequent, and ample; and from the beginning of one to the beginning of the next was 1·3 seconds. The first few movements often shewed slight irregularity of tracing, both in contraction and relaxation. Tracings, therefore, shew graphically, not only what is

evident when the movement is watched, but also that it is a long while before contraction and relaxation are normal; that, after the first one or two, each contraction is feeble for a time; and that the early contractions and relaxations are often a little irregular.

Tracings were also taken shewing the result of a single contraction of

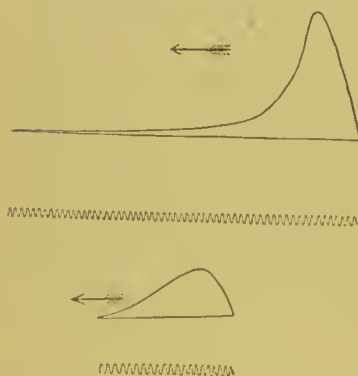


FIG. 6.—Tracings of contractions of extensors of forearm produced by the same momentary stimulus K.C.C. in a normal person and in a patient with myotonia congenita. The arrows indicate the direction in which the tracings should be read. The vibrations of the tuning-fork are 100 per second.

the extensors of the forearm induced by the galvanic current (Fig. 6). The rise occupied  $\cdot 09$  of a second, the fall or relaxation occupied  $\cdot 5$  of a second: whilst in a contraction of my own extensors obtained under precisely similar conditions the rise occupied  $\cdot 06$  of a second, and the fall  $\cdot 15$ . These figures shew very well that in Thomsen's disease the contraction and relaxation, but especially the relaxation, are much prolonged. In other experiments a tetanising current was used; and here again it was shewn that both contraction and relaxation, but especially relaxation, were much longer than in health. I made many experiments to determine the length of the latent period, because Blumenau and one or two other experimenters have stated that in Thomsen's

disease it is prolonged; I always found, however, that it was of the same length as that of a healthy person.

**Duration.**—So far as it is known the disease never passes off; on the other hand it has never been the cause of death. The stiffness usually becomes a little worse at puberty.

It is so rare for the patients to have any disease elsewhere than in their muscles that probably the association, when it occurs, is accidental. Atwood mentions a case associated with migraine, and Carrière one associated with macroglossia and congenital syphilis.

**Treatment.**—No treatment that has been employed has had any good effect. Thomsen thought he was better the more active his life. One patient said the disease lessened after she was married. Nerve-stretching has been tried, but without any good effect.

Since 1900 many atypical cases of Thomsen's disease have been recorded. The time is not yet ripe for deciding whether they should all be regarded as instances of this disease, or whether some are examples of still rarer maladies. Various names have been given to these varieties, thus: (a) Paramyotonia congenita. This is a family condition, but it differs from myotonia congenita in that the peculiar contraction is only seen in cold weather, the muscles of the eyes are especially liable to be affected, the contraction and subsequent weakness are of long duration, and the peculiar contraction is not induced by electrical and mechanical stimulation; (b) Myotonia atrophica, already alluded to; (c) Myotonia

congenita intermittens; (d) Myotonia acquisita; (e) Partial myotonia. For further information the reader should consult an article by Pelz.

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#### MYOPATHY—OR MUSCULAR DYSTROPHY

SYNONYMS.—*Primary Progressive Myopathy; Progressive Muscular Dystrophy (Erb); Idiopathic Muscular Atrophy and Hypertrophy.*

By the late C. E. BEEVOR, M.D., F.R.C.P.

Revised by FREDERICK E. BATTEN, M.D., F.R.C.P.

**Short Description.**—Under the name myopathy is comprised a group of cases which, though for some time confused with atrophies of muscles secondary to changes in the spinal cord, are now considered to be due to lesions of the muscular substance itself, the cord not being affected. Clinically they are distinguished by atrophy and hypertrophy of muscles, which differ in their grouping from the changes in the progressive muscular atrophy due to disease of the anterior cornua of the spinal cord. Frequently they occur in several members of one family of the same or of subsequent generations. In all these cases the muscles themselves are at fault, and, though the changes do not usually occur for a few or perhaps for several years after birth, the disease is essentially



congenital. Sir W. Gowers has suggested the name "abiotrophy" as indicating a defective vital endurance, and in this sense the myopathies might be included under such a title.

**History.**—The first cases described were those now known as pseudo-hypertrophic paralysis, of which instances were recorded by Sir Charles Bell (in 1830) and by Partridge (1847). Meryon, who gave a very accurate description of four boys in one family affected by atrophy with contractures, published in 1852 an account of a necropsy, in which he states that the spinal cord and nerves were carefully examined microscopically, and not the slightest trace of disease was detected in the ganglion-cells of the grey matter and the anterior roots; the only structural change observed was in the muscular fibres, which were broken down and converted into oil-globules and granular matter; of these changes he gave drawings. Meryon called the disease a granular and fatty degeneration of voluntary muscles. In 1853 Little referred to two exemplary cases of pseudo-hypertrophic paralysis, which he observed in 1847 in two brothers with enlarged calves, talipes equinus, lordosis on standing, kyphosis on sitting, and atrophy of the upper arms with large deltoids; at the necropsy the gastrocnemii were found large and fatty with traces only of muscle-tissue, but no mention is made of the spinal cord. In 1855 Duchenne published cases of progressive muscular atrophy in adults and children, and described some of these cases in adults as beginning in the trunk muscles or shoulder, and in the latter as affecting the facial muscles, and especially the orbicularis oris; but he ascribed them to lesions of the cord. Duchenne, in 1855, speaking on "atrophic musculaire graisseuse," and on a necropsy of a case by Cruveilhier, refers to Meryon's case, the figures illustrating which, Duchenne says, have a great similarity with the features he had seen in cases of "atrophic musculaire graisseuse," and he dismisses the matter with the opinion that Meryon's case was one of a "muscular affection commencing in infancy, of which state I have seen a good number, and which I will call *Paralysie atrophique graisseuse de l'enfance*," a disease which, from his description on p. 839 (*loc. cit.*), was evidently infantile paralysis.

Meryon, in 1864, described a necropsy on a second case in 1859, in which he states that not a trace of disease was found in the central nervous system, also that these cases may be recognised by the absence of any symptom of central disturbance, and that they are not the same as simple muscular atrophy, but are due to lesions of the muscles only. He says, "M. Duchenne has referred my first case to a category of disease which he designs as nervous in character, resulting from some antecedent febrile affection, and terminating in rapid recovery or in degeneration into fat of the affected muscles, and he calls this '*Atrophic graisseuse de l'enfance*,' . . . but my cases have nothing in common with these." Meryon further shewed the hereditary nature of his cases; and also stated that in one family there was an uncommon increase of the gastrocnemii. He further states, "I am induced to believe in an idiopathic disease of the muscles, dependent perhaps on defective nutrition.

Spontaneous twitchings are not apt to occur." In 1865 Enlenburg and Cohnheim examined a case after death, and found no changes in the spinal cord, and in 1871 this condition was confirmed by Charcot in a case of Duchenne's.

From these extracts it is evident that Meryon, in 1852, was the first observer to attribute these cases to idiopathic diseases of the muscles. This is all the more important as the first description of these cases has been ascribed to Duchenne, who, in 1861, described them under the name of *Paraplégie congénitale cérébrale hypertrophique*; it was not until 1868 that he recognised the malady as independent of all alteration of the nervous system, and gave it the name of pseudo-hypertrophic paralysis. Duchenne laid great stress on the hypertrophy of the muscles, which was not a prominent feature of Meryon's cases. Adams, in 1868, published several cases; and in 1876 Leyden put into a separate class certain muscular atrophies which occur in families, and called them "hereditary." In 1882 Erb described a form of muscular atrophy in young people, in whom the muscles did not give the reaction of degeneration to electrical testing, and this form he qualified as "juvenile."

Landouzy and Dejerine, in 1884, published a note, with one necropsy, on cases of the so-called facio-scapulo-humeral type, in which the spinal cord and peripheral nerves were exempt, but in which there was a simple atrophy of the muscle-fibres; and they distinguished between these cases, which they called "*Myopathie atrophique progressive*" of childhood, and the "*Atrophie progressive myélopathique*" of adults, in which the cord is involved. In 1885 these authors published a full paper on their cases. In 1884, two months after the above, Erb published a full account of the juvenile form of muscular atrophy. The best account in this country of pseudo-hypertrophic paralysis is the monograph by Sir W. Gowers (32).

Since then contributions on the subject have been numerous. Many types of myopathy have been described, and it would seem possible to divide the whole group into a very large number of "types" if slight variations are taken to indicate a "type." Since there is no sharp line of distinction between the various types, some writers would disregard them altogether. On the other hand, for the sake of clinical recognition and description "types" are convenient, and the following will be described:—(1) *Simple atrophic*; (2) *Pseudo-hypertrophic*; (3) *The juvenile*; (4) *The facio-scapulo-humeral*; (5) *The distal*; (6) *Myotonia atrophica*; (7) *Mixed and transitional types*.

1. **SIMPLE ATROPHIC TYPE.**—This form of myopathy is characterised by smallness, lack of power and tone in all the muscles of the body, without localised atrophy or hypertrophy of individual muscles or groups of muscles. The name "infantile" might well be applied to these cases, and was the title under which some examples have been described (Batten), but the name has unfortunately been used for cases of the facio-scapulo-humeral type in which the face is affected in early infancy.



Some of the cases originally recorded by Erb under the title "simple atrophic form," come in this category, and also those described by Leyden.



FIG. 7.—Photograph of a boy aged five, with the simple atrophic type of myopathy, attempting to rise into the sitting position.

Probably amyotonia congenita (*vide* p. 24) is closely related to this condition. The cases described by Haushalter in 1898 are intimately connected to this group, although the implication of the face in two of the cases shews their relation to the facio-scapulo-humeral type.

The disease is congenital or starts in early infancy, and advances but slowly, for the child may, as development takes place, learn to sit up and possibly to stand with support.

The morbid anatomy of this form does not differ from that of the other myopathies. There is no change in the central nervous system; and the muscles shew the

fatty and fibroid change, and the hypertrophy of individual muscle-fibres characteristic of the myopathies.

**Symptoms.**—The appearance of children with this disease is very uniform. They are of small make, with thin arms and legs, but though often unable to stand or walk, they can usually sit up with the legs flexed. The feet and hands often appear unduly long and, owing to the flaccidity of the muscles, can be bent at an unusual angle to the arm or leg. All movements can be performed, but in a feeble manner, and the movements of the face are perfectly good. The child learns to talk at the usual age, and intellectually is often in advance of his years. He usually adopts some strange manœuvre for getting about, sometimes he rolls round and round in his long axis in order to cross the floor, or other children continue the "buttock-walking" of infants. Usually one member only of a family is affected, but others may suffer. Cutaneous sensation is perfect. In the later stages there is often some contraction of the flexors, so that the legs cannot be fully extended (Fig. 8). The deep reflexes are usually absent, the superficial being present. The electrical reaction of the muscles is such that a very strong faradic current is required to obtain a contraction. The strong faradic current is well borne and does not seem to cause any pain. The reaction to the galvanic current is diminished, but qualitatively the response is normal. The child is usually most sensitive to the galvanic stimulation.

**Diagnosis.**—There is no sharp line of distinction between this and the other forms of myopathy; the affection of the face would bring this class in relation to the facio-scapulo-humeral type, and any enlargement of the calves into relation with the pseudo-hypertrophic type. At

present it is impossible to make any dogmatic statement as to the relation of this condition to amyotonia congenita, but some of the cases described under that title almost certainly belong to the myopathic group.

The condition must be carefully distinguished from the progressive spinal muscular atrophies of infants, which Werdnig and Hoffmann first described and shewed to be a progressive muscular atrophy due to atrophy of the cells of the anterior horns. The similarity of the two conditions is very great, and in some cases it would seem almost impossible to draw a line between those cases which are primarily myelopathic and those which are myopathic. A rapid course, together



FIG. 3.—Photograph of a girl aged twelve, with simple atrophic myopathy, shewing the general wasting of the limbs with contraction of the flexors and the long feet and hands.

with evidence of implication of the diaphragm and the muscles of phonation and deglutition, are greatly in favour of a myelopathic affection.

The prognosis is the same as that in other forms of myopathy. Although the disease is present at birth it does not prevent the development of the child from taking place, though this is always delayed and never complete. An infant with this affection is probably very late in learning to sit up, and even then cannot readily maintain its balance. The children live for varying periods of five to twelve years, and die from some accidental cause or from some acute or chronic infection.

2. PSEUDO-HYPERTROPHIC PARALYSIS.—This type is characterised by weakness of certain groups of muscles with hypertrophy of some and wasting of others. The muscles commonly hypertrophied are those of

the calf, the glutei, and the infraspinati; the muscles commonly atrophied are those of the thigh, the lower portion of the pectoralis major, the biceps, and latissimus dorsi.

**Etiology.**—*Age.*—It is essentially a disease of childhood. In some cases the child has never walked properly; in others the child is quite well till the fourth or fifth, or even the ninth or tenth year. A few cases develop about puberty. Cases have been recorded in which the disease began at twenty-four and twenty-five years of age (Green, Head), and even between thirty and forty (J. K. Fowler, Morley Fletcher).

*Sex.*—Boys are very much more often attacked than girls; this contrasts with the juvenile and facio-scapulo-humeral types which fall on the sexes about equally.

*Heredity.*—The disease is peculiar in attacking several members of the same family. In Meryon's cases, all the four boys of one family were attacked, whilst the six girls escaped. But although the women of a family escape they are able to transmit the disease to their sons, and in some recorded cases the disease has been transmitted by the female side to the third generation (Gowers). The disease does not appear to be induced or affected by social surroundings.

**Symptomatology.**—The early symptoms which the parents notice in a child affected with this disease are the frequency and readiness with which he falls down, the difficulty that he has in getting on to his feet again and in going upstairs. The increased size of the muscles is not usually observed by the friends, probably because a uniform enlargement of the muscles is regarded as a mark of strength, and atrophy as associated with paralysis. Combined with the weakness is an alteration in the size of the muscles of the limbs and trunk. The alteration in size is either in the direction of hypertrophy or of atrophy, and it is remarkable that certain muscles are prone to hypertrophy and others to atrophy, although some muscles are said to hypertrophy at first and to atrophy later; the condition which the muscle assumes at first is frequently maintained throughout.

Of the muscles which enlarge, the calf muscles, the gastrocnemius and soleus, are especially liable to be affected. They may at first be only harder than natural, but frequently they enlarge very much, as in the case of a boy aged twelve years, in whom the calf measured  $14\frac{1}{2}$  inches (Gowers); they tend to assume a peculiar shape, the posterior border of the calf presenting an elliptical shape, so that the most prominent point of the convex curve is over the middle of the calf, whereas in true muscular hypertrophy the calves are flatter. The weakness of these muscles can be demonstrated by the inability of the patient to stand on tiptoe, whereby it is made evident that the increased size is not due to increase of muscular tissue.

The anterior tibials are said to be increased in some cases, but this is certainly unusual. Of the other muscles of the lower limb, the extensors of the knee and the gluteus maximus are especially enlarged. Of the extensors of the knee the vastus externus is perhaps the most commonly



enlarged, and it is characterised by causing an abrupt projection just above the knee. The glutei are uniformly enlarged and hard to the touch. The flexors of the knee and the flexors and adductors of the hip-joint are usually atrophied. The erector spinae is in some cases hypertrophied, in others atrophied.

In the shoulder the hypertrophied muscles are the deltoid and the supra- and infra-spinati, which are nearly always enlarged; the deltoid is very much enlarged, and if it be felt during relaxation, by passively supporting the arm at right angles to the trunk, it will be found harder than natural. The condition of the supraspinatus, from its being covered by the trapezius, is more difficult to ascertain; but the infraspinatus stands out prominently as a hard mass.

Of the muscles which are wasted, the lower half of the pectoralis major arising from the sternum and the latissimus dorsi are almost invariably affected; the absence of the former is well shewn by making the patient advance both arms horizontally forwards, when on pressing the hands together the upper fibres alone of the pectoralis major will be seen to contract, and the sharp lower border of these fibres will be felt passing to the upper end of the sternum. Absence of the latissimus dorsi and pectoralis major (lower half) can also be shewn by making the patient adduct the humerus, previously raised to the horizontal line, against resistance, when no muscle will be seen going from the humerus towards the pelvic brim, and the teres muscles will stand out, and will draw the scapula forwards into the axilla, and especially if the rhomboids be weak. The absence of the latissimus dorsi and of the lower part of the pectoralis major can also be demonstrated by placing the hands in the axillae from behind and lifting up the patient, when the scapulae will be drawn upwards from the trunk to an extreme degree. The trapezius, rhomboids, and serratus magnus are usually not affected, though the last-mentioned may be wasted.

In the arm the triceps is usually hypertrophied, presenting a convex outline which is very characteristic, whilst the biceps is atrophied. In the hand and forearm the muscles usually escape, but the extensors of the wrist and fingers are sometimes slightly enlarged, and the supinator longus may be atrophied or enlarged. The intrinsic muscles of the hand nearly always escape; but examples of hypertrophy have been observed by Sachs, and enlargement of the abductor indicis by Dr. J. Taylor (61). The muscles of the face and neck are not affected as a rule, but in a few cases the tongue and masseters have been enlarged.

The weakness of the muscles gives rise to a peculiar attitude and gait. While sitting down nothing peculiar is noticed; but when the patient is told to stand up, especially from a low seat, he finds considerable difficulty in doing so. This is due in great measure to weakness of the extensors of the hips and of the knees. Also, in getting up from the supine position on the ground certain actions are performed which are quite characteristic. Instead of assuming the sitting position, the patient rotates the whole trunk by means of pressure with the arms on the

ground, so as to get on to one side; he then flexes the hips, drawing up the knees under the abdomen, and is enabled by rotating the trunk round the knees as a fixed point to get on to his hands and knees "on all-fours"; he next extends the knees by throwing the head well down between the arms, so as to bring the centre of gravity as much forwards from the hips as possible. When the knees are extended he keeps the feet fixed, travels back on his hands, and then suddenly transfers one hand from the ground to his knee and then the other hand; now he has to extend the hip, and this he does by transferring each hand in turn to a higher point along the thigh till, by suddenly throwing the shoulders back, and shifting his centre of gravity backwards, he can extend the hip and get the trunk into the erect posture. In standing the patient keeps his feet wide apart to ensure a broad basis, and in walking he has a peculiar "waddle," throwing the shoulders from side to side; this action is to enable the feet to clear the ground, and it is particularly noticed when there is paralysis of the anterior tibial muscles and of the flexors of the hips. When there is weakness of the extensors of the knee, the knee comes forward in advance of the foot, the leg being swung into the extended position before receiving the weight of the body.

Another important deformity is that of the spine, which changes its curves in the standing and sitting positions; on standing there is frequently marked lordosis, the concavity being most in the lumbar region, with a marked compensatory convex curve of the cervical and upper dorsal region, so that a plumb-line hung from the most prominent point of this upper curve would fall an inch or more behind the gluteal region; on sitting down, these curves either disappear altogether or the spine forms one curve with its concavity forwards (kyphosis).

Besides the above deformities, which are due to paralysis of the muscles, there is another which is due to the contracture of certain muscles, and notably of those of the calf (producing talipes equinus); this contracture occurs rather early in the disease, and appears to be due to the gradual shortening of the fibrous tissue of the muscle, which in these cases is much hypertrophied, and consequently it takes place only in the muscles which are enlarged.

The electrical reactions of the muscles are very important, especially from a diagnostic point of view. At first there is no alteration, but, as the muscles whether in atrophy or hypertrophy become weaker, the amount of contraction both to faradic and galvanic currents diminishes. This is because only those fibrils can contract which still retain their muscular qualities. As the disease progresses, the strength of the currents has to be increased, until finally, when there is no more muscular tissue left, the muscles cease to respond to either current. There is never, however, the reaction of degeneration.

The persistence of the knee-jerk depends upon the state of the extensor quadriceps cruris. It has been said that the knee-jerk is increased in the early stages of the disease. As the extensor cruris becomes more involved and weaker, the knee-jerk diminishes and is

finally abolished; it probably varies directly as the integrity of the vastus internus, for Prof. Sherrington has shewn that the presence of the knee-jerk in the monkey depends entirely on the integrity of this part of the quadriceps extensor. Ankle-clonus is never obtained. The superficial reflexes, such as the plantar, are obtained as long as there are any muscles to respond to the sensory stimulus, and flexion of the big toe is obtained and not extension.

Another symptom which separates these cases from progressive spinal muscular atrophy is the absence of muscular fibrillar contractions. Muscular twitching, however, has rarely been observed in connexion with myopathy (J. Taylor (62)).

Sensation for all kinds of stimulation is always intact. Sensory changes have, however, been described (Lannois and Porot).

The sphincters are not affected except perhaps at the very end of the disease.

The degree to which the muscles are hypertrophied or atrophied varies very much, and in some cases atrophy so predominates that hypertrophy exists to a slight degree or not at all.

3. THE JUVENILE FORM OF PROGRESSIVE MUSCULAR ATROPHY is characterised by weakness and wasting of the muscles about the shoulder-girdle, especially the serratus magnus, trapezius, biceps, and triceps. Erb first described it; but the earliest recorded case appears to be that of a man called Seurat, who was exhibited in London in 1825 as the "living skeleton," and is figured and described in Hone's *Every-day Book*. It differs from the preceding in that the muscles are usually atrophied, not hypertrophied; and that the onset of the disease is much later in life. Dr. Trevelyan records a family in whom five members were affected between ten and twenty. It will be described on p. 41

4. THE FACIO-SCAPULO-HUMERAL FORM OF LANDOUZY AND DEJERINE is probably the same disease as the juvenile form, but the face muscles are also affected. It is characterised by weakness and wasting of muscles of the shoulder and pelvic girdle, with wasting of the muscles of the upper arm and thigh, and by a weakness of the muscles of the face which is often present at birth.

The hereditary nature of the disease is markedly present not only in one generation, but running through several. In one instance 24 cases were distributed through five generations (Barsickow). Still, in many cases no other members of the family are found to be affected.

The sexes are about equally affected, a point of distinction from pseudo-hypertrophic paralysis.

According to Erb's account of his cases in 1882 and 1884, the disease attacks children or young people about the time of puberty, and always begins before the twentieth year. The muscles first affected are those of the shoulder-girdle and of the upper arm; and the list includes the pectorales major and minor, trapezius, latissimus dorsi, biceps, brachialis



anticius, supinator longus, triceps, later the thigh muscles, and the anterior tibial muscles and peronei. The face is not affected, and the forearm muscles, with the exception of the supinator longus, escape.

The account given of their cases by Landouzy and Dejerine in 1884 is, that they were described by Duchenne (17) originally under the name of progressive muscular atrophy of childhood, but were confused by him with cases of spinal cord origin; these authors consider them to be myopathic as opposed to the myelopathic progressive muscular atrophy of adults.

The disease begins most often in infancy, and in the face; it may, however, begin in youth, in adult, or in advanced age. When it begins in the face the orbiculares palpebrarum and oris are the first to be attacked, and thus arises a peculiar physiognomy, which gives to the face when at rest a gaping expression (*facies béant*): the lips are prominent, and the forehead smooth; the eyeballs are apparently prominent, and on movement of the face a retraction of the angles of the mouth without elevation of the upper lip produces a curious sad expression, the immobility of the features contrasting with the animation of the eyes.



FIG. 9. Characteristic winging of the scapulae in the facio-scapulo-humeral type, due to weakness of the serratus magnus and trapezius. This patient's son was similarly affected, and had never been able to close his eyes.

After the face, the atrophy nearly always attacks next the upper limbs, and especially the muscles about the shoulders and arms; hence the name "facio-scapulo-humeral" palsy.

The muscles which escape are the supra- and infra-spinati, the sub-scapularis, the flexors of the wrist and fingers, and the muscles of the eyes, and those for mastication, swallowing,

and speech. The muscles are atrophied from the beginning, and there is no hypertrophy.

Fibrillar contractions of the muscles are absent, and idio-muscular contraction disappears or is much diminished. Electrical excitability of the muscles is modified quantitatively to both forms of current, and the normal formula is diminished, but it is not inverted; that is to say, there is no reaction of degeneration. As a rule the tendon-reflexes do not disappear till the muscles are very much atrophied.

In youth and adult life the disease is said to be rarer than in childhood, and does not always begin in the face; it may start in the upper limbs, or even in the lower limbs, and the face may or may not be affected later.

According to Landouzy and Dejerine, their facio-scapulo-humeral form is quite distinct from the juvenile form of muscular atrophy of Erb. They state that their disease more often begins in the face than not;

that in progressive atrophy of myelopathic (or spinal cord) origin the face is never affected, and that atrophy of the muscles of the face is the only clinical character by which the disease can be recognised at once.

In Erb's juvenile form, the biceps, triceps, and supinator longus are the first to be affected; the pectoralis major, the latissimus dorsi, and the serratus magnus are next affected. Since, however, the deltoids, supra- and infra-spinati are often preserved, the scapulae project very much at their posterior borders when the patient endeavours to hold his arm out in front. The trapezius is especially liable to be affected along its whole breadth, including the highest clavicular fibres, whereby the slope of the neck to the shoulders is altered—thus producing a condition which is very characteristic of myopathies, and sometimes the sterno-mastoids are wasted. The forearm, with the exception of the supinator longus, escapes, and so also do the hand muscles, except in rare cases.

The back and trunk muscles are frequently much affected, and give rise to the following deformities of the spine:—(i.) When on standing up there is marked lordosis, so that a plumb-line let fall from the most prominent point of the dorsal spine hangs several inches behind the sacrum, whereas on sitting down the lordosis disappears, or is transformed into kypbosis, the erector spinae muscles are at fault. (ii.) When with extreme lordosis the sacrum projects back so much that the plumb-line does not fall without the sacrum, it will be found that the pelvis is tilted forwards; and in addition to weakness of the erector spinae there is weakness of the glutei: in this case the lordosis disappears on sitting down. (iii.) When the condition of lordosis does not disappear on sitting down, this is due to superadded weakness of the recti abdominis muscles, which are unable to keep up traction on the thorax from the pelvis in front to flex the spine, and to prevent the abdominal wall from projecting forwards. The trunk in these extreme cases remains flexed and assumes a swan-like appearance, and the walk is very like the waddle of that bird. In the lower limbs, besides the glutei, the adductors and the flexors of the hip are often weak, and especially the quadriceps extensor cruris, which may be much wasted; below the knee the anterior tibial muscles suffer occasionally.

In the facio-scapulo-humeral group the orbicularis palpebrarum is so weak that the patient cannot close the eyelids completely. He sleeps with his eyes open, and soap gets into the eyes in washing the face. The eyelids can be opened with the slightest pressure of the finger, and there is no power of "screwing-up" the eye by the outer fibres of the orbicularis. The levator anguli oris and the orbicularis oris are paralysed, so that there is no power to elevate the upper lip, or to purse up the lips as in whistling. In connexion with the affection of these muscles of the face, it is important to note that the muscles of the eyeball escape, and also that the tongue is not involved. Mendel's hypothesis that the orbicularis palpebrarum gets its nerve-supply through the facial nerve from the third nucleus and the orbicularis oris from the hypoglossal nucleus

can no longer be used in the differential diagnosis of these cases from those due to a central lesion. All the evidence, both morphological and anatomical, is against such an hypothesis, and the orbicularis palpebrarum and orbicularis oris are almost certainly supplied from portions of the nucleus of the seventh (Bruce and Pirie, and Harman).

In both these forms, as in pseudo-hypertrophic paralysis, there are no fibrillar contractions of the muscles; the electrical reactions to both forms of current become less, but there is never any reaction of degeneration; the knee-jerks are retained as long as there are any muscle-fibres left in the vastus internus to respond, and then only are they lost. Sensation is never lost, and the sphincters are not affected.

Dr. T. Buzzard describes a type in which the ilio-psoas group of muscles was primarily affected; the patient shewed some weakness of the facial muscles, which would probably bring the case into relation with the Landouzy-Dejerine type.

5. DISTAL MYOPATHY.—This type of myopathy was described by Sir W. Gowers in 1902; examples have also been recorded by Spiller, Dejerine and Thomas, and Campbell. The characteristic feature of this type is the weakness and atrophy of the muscles below the elbow and knee, whilst the proximal muscles remain well developed.

6. MYOTONIA ATROPHICA.—This condition is characterised by the rare association of muscular atrophy with a slow relaxation of muscles after voluntary contraction. The muscular atrophy has a distribution which is peculiar. There is weakness of the facial muscles (myopathic face), atrophy of the sterno-mastoids, the vasti of the thighs, and the dorsi-flexors of the feet. The slow relaxation of muscles affects most frequently the flexor muscles of the hand, and the more forcible the muscular contraction the slower the relaxation. This distribution of muscular atrophy has been found in 15 out of the 27 recorded cases. The condition affects members of the same generation, and there is some evidence shewing that it is transmitted from parent to child. The male sex is much more commonly affected than the female.

The name myotonia atrophica was first suggested by Rossolimo, but Noques and Sirol and Hoffmann had previously published cases of this condition under the title of Thomsen's disease with muscular atrophy.

**Etiology.**—No cause for the condition has been found. It has been attributed to severe cold and to acute illness.

**Age.**—The age of the recorded cases varies greatly, the youngest case at present recorded was fifteen, but in the majority of instances the symptoms first appeared between the ages of twenty and thirty.

**Morbid Anatomy.**—Steinert has quite recently made a complete examination, and has shewn that the condition of the muscles is the same as in other myopathic cases. He found, however, degeneration of the posterior columns in the lumbar region.

The course of the disease is usually very chronic and prolonged. In



some cases no advance appears to be made in the symptoms during many years; in others the patients are hardly aware of their disability until they come under examination, and when pointed out to them they attribute it to a "family failing."

The following may be taken as a fairly characteristic example of the disease:—A man, aged forty, first noticed wasting of his thighs when thirty-two years old. This caused him no inconvenience till two years later, and then his knees would suddenly give way when walking. There had been a certain stiffness of the legs and difficulty in starting to walk. For many years he has had difficulty in relaxing his grasp. This difficulty passes off after repeated movement. He is the second of a family of three—his elder brother died of a nervous disease said to be "locomotor ataxia," and his sister, who is younger, has similar symptoms to her brother; these, however, are so slight that they give rise to but little inconvenience. The distribution of the muscular atrophy is similar in the brother and sister. The man has the characteristic weakness of the facial muscles. He is unable to close the eyes forcibly, and there is weakness of the orbicularis oris. Both sterno-mastoids are completely atrophied. There is no wasting of the shoulder or upper-arm muscles, but the forearm muscles are thin and their power diminished. In the thighs there is extensive atrophy of the vastus internus and externus, but the other muscles of the leg are well developed. The knee-jerks are absent. When the patient is asked to grasp an object he does so with a fair amount of force, but if asked to relax he has difficulty in doing so owing to the slow relaxation of the flexor muscles of the hand. In some cases paralysis of the vocal cords has been described.

The most striking feature with regard to the *electrical reaction* is the very marked diminution of irritability of the muscles generally to the faradic current. This corresponds to that which is commonly found in the myopathic condition. The contraction produced in the flexor muscles of the fingers is fairly brisk, but the relaxation which follows is relatively slow, lasting about three to five seconds. It cannot be said that the muscles give the true myotonic reaction as described by Erb (*vide* p. 28).

7. MIXED AND TRANSITIONAL TYPES.—Besides the six types mentioned above there are many intermediate forms which serve as connecting links between these types. Their characteristic is that they possess two or more of the most marked features of other types, *e.g.* a child with pseudo-hypertrophic paralysis may shew a "myopathic face," or a facio-scapulo-humeral type may have hypertrophy of the calf muscles.

COURSE.—The course of these diseases, taken as a whole, is very slow and gradual, but the degree to which the atrophy reaches in extent and severity differs in the several groups, and this difference seems to depend on the age at which the disease begins. Pseudo-hypertrophic paralysis probably runs the most rapid course, but even this often lasts ten to fifteen years. It is remarkable that those rare cases which begin in adult

life, and present hypertrophy of some of the muscles, do not run the unfavourable course of ordinary pseudo-hypertrophic paralysis.

Cases of Erb's juvenile form run a more favourable course than those of ordinary pseudo-hypertrophic paralysis, and the atrophy progresses to a certain degree and then often remains stationary; cases are met with in adults which have not materially altered for eighteen or more years. Also in the facio-scapulo-humeral series the course depends much on whether the disease began in childhood or after puberty, as in the latter event the disease makes but little progress and the patient may live many years.

The course and duration of pseudo-hypertrophic paralysis vary much in different cases, and the disease may be divided into two stages, the second stage being reached when the patient is no longer able to walk. After the onset of the second stage, which may occur when the disease has lasted a few years, the patient rapidly deteriorates. It is not usual for the patient to die from the disease itself, but if he gets a slight attack of bronchitis or pneumonia the respiratory muscles are so weak that he succumbs to the pulmonary disease; these patients seldom live over the twentieth year.

**PATHOLOGY OF THE MYOPATHIES.**—The morbid changes are in most cases entirely confined to the muscles. Changes have been found in the spinal cord, the spinal roots, and the peripheral nerves. In one case (14) the anterior cornua of the cord were normal except at the last dorsal segment, where an area of granular disintegration in the intermediate substance was found on each side. A definite diminution in the number of the ventral cornual cells has been noted (Erb and Schultze, Heubner, Schultze, Strümpell, Kollarits, Lorenz, Rocaz and Cruchet, Port, Ingbert, and Holmes); and slow degenerative changes only have been described (Kahler, Priesz, Frohmaier, and Sabrazès and Breugues). In most of the cases changes were seen also in the anterior roots and in the peripheral nerves. According to Dr. G. Holmes's examination of a case under the late Dr. Beever's care the lesion in the lower motor neurons was an acquired and not a developmental defect; the nature of the cell changes, the slight secondary gliosis of the ventral horns, the definite evidence of loss of fibres in the ventral roots and peripheral nerves, as well as the increase of connective tissue in the nerves, point to this conclusion. The histological changes in the ventral cornua are quite distinct from the degenerative changes of spinal amyotrophies.

The muscles are found after death either to be very wasted, or, if they have been enlarged, to have diminished to about the normal size. They are paler than natural, and in extreme cases, when cut across, give the appearance of a fatty tumour without any trace of muscle.

When examined under the microscope the muscle-fibres, when moderately affected, are diminished in size and numbers, and are separated by fat-cells and by bands of fibrous tissue. The relative amount of fat and fibrous tissue differs in different muscles. The change in the muscle



is primarily interstitial, and consists of an overgrowth of fat and nucleated fibrous tissue between the muscle-fibres, and secondarily in the muscle-fibres, which become narrow and irregular in shape. The transverse striation is at first preserved, but it becomes more faint, and finally disappears, and the muscle undergoes a granular degeneration. Rarely the muscle-fibres shew fatty degeneration, longitudinal striation, fissuring, vitreous (waxy) degeneration, or vacuolation (Gowers). According to Duchenne, the sheaths of the sarcolemma appear to contain fat-cells which are really derived from the surrounding connective tissue, and which otherwise differ from the fatty granular condition characteristic of

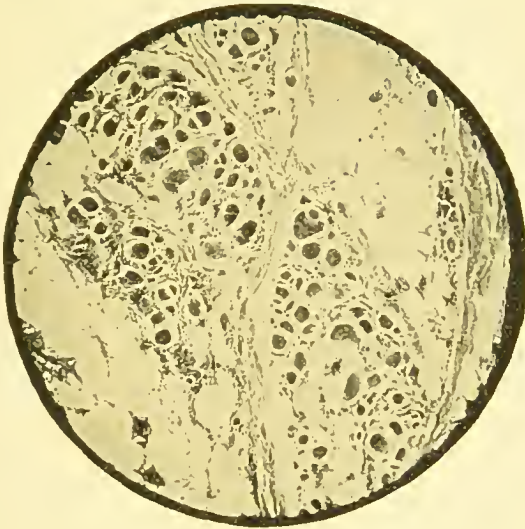


FIG. 10.—Transverse section of a portion of pseudo-hypertrophic muscle showing the typical changes, viz. atrophy of muscle-fibres, hypertrophy of some fibres, increase of intermuscular connective tissue, increase of nuclei, and excess of adipose tissue within the muscle. Magnified 30 diameters; the large fibres measure 0.1 mm. in diameter. The normal muscle-fibres of an adult measure .06 mm., and those of a boy eight years old .02-.04 mm.

fatty degeneration of muscle; and the interstitial connective tissue is not produced by fibroid changes of the muscle.

In a late case of pseudo-hypertrophic myopathy Ballet and Laignel-Lavastine found the characteristic changes in the muscles, and that the peripheral nerves did not shew any indication of a neuritic process in the cervical enlargement. In the spinal cord there was almost complete absence of the anterior cornual cells; such cells as persisted were not deformed but simply atrophic, there being no sign of chromatolysis, pigmentation, or neuroglial proliferation. In the motor cortex the Betz-cells were usually globular and deformed. The atrophy of the cells was regarded as secondary to the muscular change.

The case on which Landonzy and Dejerine based their original description of the facio-scapulo-humeral type in 1874 died in 1902 at the age of forty-five years; the pathological examination shewed the most advanced atrophy of the muscles, some, such as the biceps, being very small and of

a greyish-yellow colour. Microscopically no striation could be seen in the muscle-fibres. No trace of muscular fibres could be found in the orbiculares oris and palpebrarum. Both macroscopically and microscopically the nervous system was practically normal. The skiagram of the bones shewed unusual translucency (Landouzy and Lortat-Jacob).

The muscle-fibres have been removed for examination during life by incision by Billroth, or by a harpoon invented by Duchenne, and some of the muscle-fibres so removed have been found actually larger than normal (Gowers). It seems, therefore, that the enlargement of the muscle may be due to genuine hypertrophy of the muscle-fibres as well as to the overgrowth of fat. The change in the muscle does not affect all the fibres at the same time, so that some fibres may be hypertrophied and others may have passed on to the next stage of atrophy. On the other hand, according to Erb (25), the changes are primarily in the muscular substance itself, those in the interstitial tissue being secondary, so that the muscle-fibres hypertrophy, their nuclei increase, they are enlarged, and subdivision occurs. Soon the muscle-fibres atrophy and disappear, and this is attended by increase of the connective tissue with proliferation of nuclei. In this tissue fat appears, and on this depends whether the muscle is atrophied or hypertrophied.

From the changes found after death, there is strong evidence that this disease in its various forms must be regarded as an idiopathic disease of the muscles, and independent of any changes in the spinal cord or nerves. Erb, however, considers that his juvenile form is not a pure myopathy, but depends on structural or functional changes in the trophic cells of the anterior cornua. Strümpell also believes that the changes in the muscles depend on a defect of trophic influences, so that whereas progressive spinal muscular atrophy is due to anatomical change in the trophic centres in the cord, this form is caused by a functional disturbance in the cord. Against the view that the cell changes are primary it may be urged that the muscular changes are advanced out of all proportion to the changes in the cornual cells.

It has also been thought that the changes in the muscles and in the anterior cornual cells are both due to the same cause, but this is incompatible with the occurrence of cases of myopathies in which there are no nervous changes. The most probable explanation is that originally given by Meryon, to the effect that the condition is due to an idiopathic disease of the muscles, and that the changes observed in the anterior cornual cells are secondary to the primary changes in the muscles. Whether this cell change is due to want of function as the cells are no longer employed, or to irritation of their terminal axis-cylinders by the fibrous changes in the muscles, is not known.

The difference in the condition assumed by the muscles, that is hypertrophy or atrophy, seems to be due to the amount of fat and fibrous tissue respectively. Those muscles in which the changes are in the direction of formation of fat are the enlarged muscles, and they are liable subsequently to atrophy; those in which fibrous changes occur

become hard and diminish in size; whilst in a third group, such as the lower half of the pectoralis major and the latissimus dorsi, the muscles seem to waste and disappear without the formation of fat or fibrous tissue. It is difficult to explain why the muscles should behave in this way; but from the tendency of the disease to attack several members of the same family, and in some instances to pass from parent to child, it seems that the disposition of the muscles to undergo this fibrous and fatty overgrowth is an inherited quality.

The reason why certain muscles should be singled out by this disease has been given by Babinski and Onanoff, who explain it by the relative times of development of the different muscles. Thus, in examining a five months' fetus, they ascertained that the muscles which were the most developed included the supinator longus, serratus magnus, latissimus dorsi, rhomboids, middle and lower part of trapezius, orbicularis oris, quadriceps extensor cruris, tibialis anticus, and, to a less degree, the deltoid, biceps, triceps, infraspinatus, subscapularis, and crural muscles; whilst the hand muscles were least developed. As the muscles ranked first are those which are particularly affected in myopathies, the authors conclude that the muscles, which are the first to be developed, are the first to undergo degeneration in these diseases.

In the hypertrophied muscles the arteries and veins are said to be increased and surrounded by foci of embryonic cells. An endarteritis is thus produced which causes a narrowing or blocking of the vessels (Babes).

The intramuscular nerves have been found intact by most observers (Blocq and Marinesco), but slight changes have been described by Fürstner, by Babes and Sacara-Fulbure, in the motor nerve-endings. The histological methods by which the motor nerve-endings can be examined are so imperfect and uncertain that little reliance can be placed on these observations. Changes in the axis-cylinders of the peripheral nerves have been found in various places by Gombault, especially near the muscles, where these structures had completely disappeared, whilst the cells of the anterior horns were healthy. The muscle-spindles are not altered (Batten). Prof. Grünbaum, however, has described some change in the muscle-spindle in pseudo-hypertrophic muscle. A diminution in the excretion of creatinine has been noted in pseudo-hypertrophic muscular dystrophy (Spriggs).

The cause of the muscular lesions has been ascribed by Babes to the changes in the vessels described above, on which their diminished nutrition ensues. The thickening of the vessel-walls is a very characteristic feature in all sections of myopathic muscle.

**DIAGNOSIS.**—The diagnosis of the various types of myopathy from a progressive muscular atrophy of spinal origin is in some cases simple, in other cases a matter of the greatest difficulty. In a case which presents the characteristic symptom-group of pseudo-hypertrophic paralysis, of the facio-scapulo-humeral type, or of the other groups already described, no difficulty should arise. But it is very different with the numerous



atypical and intermediate cases which occur. The occurrence of the affection in several members of a family, although in favour of a myopathic rather than a myelopathic lesion, cannot be used as a diagnostic criterion, for it is well known that some typically myelopathic diseases are familial; for example, the Werdnig-Hoffmann, the peroneal type of muscular atrophy, and Friedreich's disease. Points in favour of a myopathic affection are a slowly progressive symmetrical wasting of muscles not corresponding to those supplied from a spinal segment or nerve-trunk, the absence of sensory impairment, the absence of a typical reaction of degeneration, and the absence of fibrillar contraction in the muscles.

Too much stress must not be placed on any one of the above points, for fibrillar contractions may occur in myopathic cases (62), and the electrical reaction may approximate very closely to the reaction of degeneration. We should, however, hesitate to accept as a case of myopathy one with any alteration of sensation. But Lannois and Porot (45) have described a case of myopathy which had had considerable sensory change. The patient also suffered from pain in the limbs. The difficulty in diagnosis in some cases is shewn by the pathological examination of a case of progressive atrophy of the interossei muscles of the hand observed by Dejerine and Thomas for thirty years in an old woman who died when eighty years old. In this case no change was found in the spinal cord, and the muscles presented changes consistent with a primary myopathic condition.

With regard to the *differential diagnosis of the various myopathies*, many writers urge that there is no hard and fast distinction between these various types, and that all cases of myopathic atrophy should be classed together. Whilst admitting the truth of this, there is much to be gained by the division of the myopathic cases into clinical types. How far these types should be multiplied is a point that may well be considered, but the types above described are well established.

**PROGNOSIS.**—As stated above, pseudo-hypertrophic paralysis is the most fatal, the patient usually dying from some pulmonary complication before the age of twenty; whilst the facio-scapulo-humeral type and Erb's juvenile form may be consistent with life for many years. In the simple atrophic type life is seldom prolonged beyond the age of twelve. In the distal type and in myotonia atrophica life is but little shortened. As regards the muscles, those which have been attacked never recover. Although this statement is practically true, Erb has described a case of myopathy of the juvenile type in a girl aged seven years, in whom in three years recovery took place, and six years later no recurrence of the disease had taken place. Jendrassik and Marina also consider that recovery is possible. Myopathy, however, must be regarded as a slowly progressive disease, the rate of progress varying in the different forms. Sometimes the disease is stationary for years, and the patient follows his occupation without difficulty.

**TREATMENT.**—As the disease is probably due to a congenital defect

in the muscles themselves, it is difficult for therapeutics to have much effect.

Light massage and exercises, with galvanism and faradism to the spine and affected muscles, together with baths, should be used, and it was under this treatment that recovery took place in Erb's case. The muscles should be exercised both passively and actively: passively, by means of massage to the affected muscles, manipulation of the joints to prevent contracture, and by faradising the affected muscles; actively, by getting the patient to perform certain movements short of fatigue every day. He should be encouraged to walk as long as possible, as it has been observed that the subjects of pseudo-hypertrophic paralysis always get rapidly worse when they cease to be able to walk. For this purpose it is advisable to recommend tenotomy when the contracture of the calf muscles is sufficient to prevent walking, and when at the same time the other muscles of the leg are capable of the appropriate movements. No drug has been found to arrest the disease, and the best treatment is to keep up the health and strength by tonics and cod-liver oil. Phosphate of iron, arsenic, phosphorus, and strychnine may also be given to improve the general condition, but they are not known to have any specific action upon the affected muscles.

C. E. BEEVOR, 1899.

F. E. BATTEN, 1910.

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## MYASTHENIA GRAVIS

SYNONYMS.—*Pseudo-paralysis Myasthenica*; *Asthenic Bulbar Palsy*; *Erb's Disease*.

By E. FARQUHAR BUZZARD, M.D., F.R.C.P.

**History.**—It may be said, without fear of contradiction, that before 1900 very few medical men in this country had ever heard of the disease under any of its synonyms, which now occupies a well-established position among the more serious morbid disturbances of neuro-muscular function, and is generally known as myasthenia gravis. Although continental writers, especially in Germany, anticipated the English medical profession in their recognition of a distinct bulbar disease characterised by the absence of anatomical changes in the central nervous system, three cases of the condition were recorded in English literature by Willis (1685), Bazire (1867), and Sir S. Wilks (1877) before 1878. In that year Erb drew attention to a symptom-group of which ptosis, weakness of the jaw and neck muscles and, to a less extent, of the tongue and extremities, were the distinguishing features. Goldflam (1893) pointed out the ready exhaustion of the muscles in voluntary effort, and Jolly (1895), who observed the same phenomenon under the influence of faradism, introduced the term "myasthenic reaction" and called the disease "Pseudo-paralysis myasthenica." Meanwhile additional instances of the disorder were reported in this country (Lauriston Shaw, Dreschfeld). The appearance in 1900 of an exhaustive monograph on the subject by Drs. Harry Campbell and Edwin Bramwell, who had observed 9 cases, stimulated the profession here to realise the importance of the subject, and a survey of English medical literature from that time to the present

demonstrates beyond doubt that myasthenia gravis is sufficiently common to merit more general attention and recognition than it has received.

Any knowledge which we possess of the morbid anatomy of the disease is of still more recent date. Guided by the observations in a case published by Laquer and Weigert, it was subsequently shewn by Goldflam, Hun, Burr, Link, and myself, that investigation of the muscles and other organs was far more fruitful than that of the nervous system; these results have been fully confirmed by Marburg, Frugoni, Mandlbaum and Celler, and others.

**Etiology.**—Myasthenia gravis attacks the sexes equally, and, although most common between twenty and forty years of age, it has been described in a child four or five years old, as well as in a man close on threescore years and ten. It is not a familial disease, and has not any special affinity for the members of so-called neuropathic families. The plea that it has a congenital basis was formulated by Oppenheim; and bifid uvula, unilateral congenital ptosis, polydactyly, webbing of toes, and micrognathia have been noted in its victims, but there is hardly sufficient evidence to justify undue emphasis on this point. Although the onset of symptoms has followed infective diseases (such as influenza, enteric or scarlet fever), prolonged exertion, chill, emotional excitement, abdominal disturbances, and menstruation, there has been nothing to warrant the assumption that any of these are important factors in producing the disease.

Myasthenia gravis has been associated with such rare conditions as Banti's disease and angioneurotic oedema in unique instances; on the other hand its comparatively frequent association with Graves' disease has provoked considerable comment. Meyerstein, Oppenheim, Kalischer, Brissaud and Bauer, Goldflam, Rennie, and others describe examples of this combination, and the occasional occurrence of ocular palsies in exophthalmic goitre has not escaped remark in the same connexion.

It is obvious that in a disease common to either sex pregnancy, in itself, cannot be an etiological factor of primary significance; at the same time the relation of this physiological state to the evolution of myasthenia gravis in individual cases, and the remarkable way in which pregnancy may influence the disease, are sufficiently striking to prevent the omission of a reference to pregnancy in a consideration of the etiology of the disease, and to necessitate a return to the subject under the head of "Pathogenesis." So favourable was the influence of pregnancy on the symptoms in a case of Goldflam's that the patient declared "to be always well, she would have to be always pregnant." Improvement during the gravid state has been noted in other cases; on the other hand, the termination of pregnancy, or the end of lactation, has been associated with severe relapses, and, in certain instances, with a rapidly fatal result.

Although it is impossible to suspect that exposure to inorganic poisons is responsible in the ordinary way for myasthenia, yet, from the etiological point of view, it is interesting to recall a case published by Sir W. Gowers. The patient displayed many characteristic symptoms



of the disease while working in an atmosphere vitiated by petrol fumes, recovered when he was removed from their influence, and relapsed on re-exposure. In a case under my care myasthenic symptoms followed a severe poisoning due to the fumes of a closed stove; the patient recovered for a time, but relapsed without any obvious cause other than that of general ill-health.

**Morbid Anatomy.**—Our knowledge of the morbid anatomy of myasthenia gravis is very recent and probably, as yet, incomplete. Until the end of the nineteenth century no constant changes had been found in the cases examined, and the investigation of the nervous system in fatal cases had only occasionally demonstrated slight, sometimes doubtful, chromolytic or other degenerative processes in a few of the bulbar or spinal motor cells. In addition, 2 cases presented developmental abnormalities in the form of unusual septa or reduplications of the central canal or aqueductus Sylvii. In 1901 Weigert and Laquer published a case with a so-called lymphosarcoma of the thymus and what were assumed to be metastases in the skeletal muscles. This discovery sufficed to draw attention to tissues other than those of the nervous system, and Goldhamer reported a somewhat similar case. Since 1903 numerous additions to our knowledge have been made, and at the present time it is justifiable to say that there are constant morbid changes associated with the disease.

The presence of small deposits of mononuclear lymphocyte-like cells (which I designated as lymphorrhages), not only in the muscles but in most of the organs and tissues of the body, appears to be a constant feature now that search is made for them. In addition there are other pathological changes to which reference must be made in dealing with the various tissues *seriatim*.

**Nervous System.**—In the large majority of cases the central and peripheral nervous systems have been found free from demonstrable disease, although every part has been repeatedly examined by the most recent histological methods. In addition to rare instances of developmental abnormality already alluded to, a few cases are recorded in which lymphorrhages have been seen in nervous tissues. In one of these cellular deposits were found in the posterior-root ganglia of the cord, in another similar appearances were met with in the medulla oblongata, but in neither case were they large or numerous. Marburg has also described masses of what he considers to be coagulated lymph in the cord, medulla, pons, and roots of the facial nerves. Recent haemorrhages have often been noted, but these are quite common in any form of disease in which the fatal termination has been attended by respiratory difficulties.

**Muscles.**—Lymphorrhages are more commonly described in the muscles than in other organs, possibly because they have been more thoroughly investigated. The constituent cells are scattered in clumps between the muscle-fibres and generally in the immediate neighbourhood of a capillary vessel. There may be a serous as well as cellular exudate. The size of a lymphorrhage varies considerably; it may be very minute



or it may be sufficiently large to be detected in a stained section by the naked eye. They have been demonstrated in many skeletal muscles,

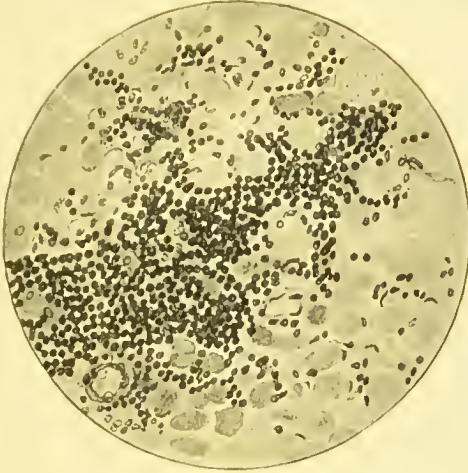


FIG. 11.—Section of ocular muscle shewing a large lymphorrhage in the midst of healthy muscle- and nerve-fibres.

in the ocular muscles and in the myocardium, although it may be

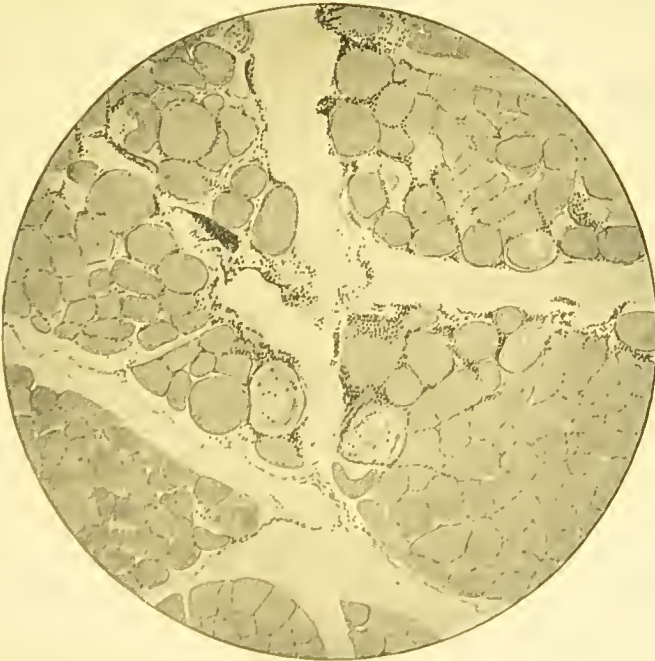


FIG. 12.—Section of a skeletal muscle shewing a rather unusual form of lymphorrhage. The cells have invaded muscle-fibres in places, and the fibres shew various degrees of degeneration.

necessary to examine very many sections to prove their existence. Speaking generally, the lymphorrhages are found in the midst of healthy

muscle, although in some instances recorded by myself, and in two others by Frugoni and Marburg, the neighbouring fibres had undergone degenerative changes and had been invaded by the cells. In the latter cases the cellular exudates differed from ordinary lymphorrhages in that they consisted of cells with oval nuclei, many of which shewed mitotic division. Frugoni believed that the cellular foci contained some of the *Tochterplasmazellen* of Unna as well as the plasma-cells.

In addition to the presence of lymphorrhages the muscle-fibres in cases of myasthenia are wont to display early changes in the form of plasmatic swelling, proliferation of sarcolemmal nuclei, possibly hyaline and granular degeneration; occasionally distinct evidence of muscular atrophy, strongly resembling that seen in amyotrophic lateral sclerosis, has been forthcoming. Unless the atrophy is marked, the muscles do not shew any abnormality to the naked eye.

*The thymus gland* is often the seat of morbid changes, although in other cases it is only represented by the remnants of lymphatic tissue characteristic of the organ in adult life. The abnormal conditions may be divided into three classes: (1) Simple hypertrophy, (2) hypertrophy with degenerative and proliferative changes, and (3) new growth. In the first class may be included those cases in which the gland, not having undergone the ordinary regressive changes, is as large or larger than that of infants. In other respects it may be perfectly normal or it may differ from the gland of a child in the absence of eosinophil cells along the septa and around the blood-vessels. Degeneration of Hassall's corpuscles and hyaline changes have also been described. The second class embraces the instances of large glands which have become almost unrecognisable owing to change in size, shape, or consistency. A good example of this may be cited from a case in which the gland weighed over 59 grams, the upper half resembling a bag containing thick creamy material, and the lower half being converted into a multilocular cyst with slightly turbid watery contents. In the third class must be placed those tumours which have been called lymphosarcomas, although there is some doubt as to how far that terminology is justified in view of our more recent knowledge concerning the cellular deposits in other parts, and of the fact that these cannot, in most cases at any rate, be regarded as metastases. In the same category may be included the perilymphatic lymphangio-endothelioma of the thymus described by Mandlebaum and Celler.

*Thyroid Gland.*—As a rule this organ does not present unusual features, except when the disease has been associated with exophthalmic goitre. Lymphorrhages have been found in several instances, and interstitial fibrosis, colloid degeneration of the fibrous stroma, proliferation of the epithelium, with formation of new vesicles, and enlargement of spaces as in simple goitre have also been noted.

*Pituitary Body.*—A large adenoma of the glandular portion was present in a case described by Tilney, but usually the pituitary body is normal.



The liver may be the seat of numerous lymphorrhages, especially in the neighbourhood of the biliary ducts, but also in between the liver cells. Serous, as well as cellular, exudation is present, and a moderate degree of fatty change of the hepatic tissue has been observed.

The adrenals in several instances have presented lymphorrhages resembling in all respects those found in the muscles and other organs. Beyond slight local parenchymatous changes in the neighbourhood of cellular deposits, there are no other variations from the normal.

The bone-marrow is, generally speaking, free from notable changes. In an unpublished case the non-granular cells were in excess.

*Pancreas.*—Lymphorrhages do not appear to be of frequent occurrence in the pancreas; but in one instance I observed a very curious result. A large lymphorrhage had so disorganised a small lobule of the gland that auto-digestion had taken place. Within this area necrotic pancreatic cells were mixed with the lymphocytes, although neighbouring lobules presented a perfectly healthy appearance. The lymphorrhages had probably taken origin from the interlobular connective-tissue septum and spread into the glandular substance.



FIG. 13.—A small lymphorrhage in a suprarenal. No obvious change in the glandular tissue.

*Kidneys.*—It is unusual to find anything abnormal in the kidneys, and they are generally recorded as healthy. In 1 case I found a very definite lymphorrhage involving a glomerular capsule, which could be traced through a series of sections.

The lungs may be the seat of morbid changes associated with terminal affections, but have probably not often been searched for microscopic changes of myasthenic origin. I have seen a large lymphorrhage in the peribronchial connective tissue round a small tube.

The blood and cerebrospinal fluid have frequently been examined in cases of myasthenia both during life and after death, but without disclosing any characteristics of import. Moderate lymphocytosis of the cerebrospinal fluid has been recorded.

To summarise the morbid changes: (1) Hypertrophy, degeneration, or new growth of the thymus are common, but not constant, incidents. (2) Lymphorrhages are of constant occurrence and probably of universal distribution, their more frequent discovery in the muscles being easily accounted for by the more careful examination of those organs and by their relatively enormous bulk. Their numbers vary considerably in

different cases and in different regions. Although they cannot be traced directly to lymphatic vessels, they are constantly found in situations where their origin from the lymphatic system is certainly not impossible. They are often unaccompanied by any changes in the tissues in which they are found; when changes occur they are purely local and probably mechanically produced. (3) Slight degenerative changes in muscle-fibres are commonly, and well-marked muscular atrophy only occasionally, found in the disease.

**Pathogenesis.**—Although the available data upon which to found a reasonable pathogenetic hypothesis for myasthenia gravis are still meagre both in quantity and quality, there have not been wanting, even in the past, authors bold enough to attempt the task. Oppenheim, for instance, was content to regard the condition as a neurosis, possibly of congenital origin. Such a designation was perhaps justifiable so long as no constant morbid anatomy was known; in view of later knowledge it must be discarded, together with the supposition that congenital anomalies form a universal feature of the disease.

More recent writers have blamed thymic and other tumours for the production of circulating poisons capable of modifying profoundly the normal activity of the neuro-muscular mechanism. Although thymic enlargements, simple or neoplastic, are sufficiently common in the disease to excite marked attention, their inconstancy requires that they should be relegated to a secondary position in relation to pathogenesis; they may perhaps be regarded as belonging rather to the morbid manifestations than to the essential pathological factors of the disease.

The view put forward by Kauffmann that myasthenia can be ascribed to a metabolic insufficiency of the hepatic function, and the hypothesis advanced by Chrostek that it depends on hypersecretion of the parathyroid glands, demand further investigation and a more convincing array of facts to ensure either of them gaining general acceptance. They are evidence, however, of the steadily growing opinion that the difficulties of the problem can best be met by assuming some auto-intoxication or metabolic perversion, some disturbance of the balance of power in the world of the internal secretions.

Lymphorrhages, which constitute the most constant feature of the morbid anatomy of the disease, might be expected to bear some causal relation to the clinical phenomena, and it has been suggested that they may produce sufficient obstruction in the lymphatic system to impair seriously the normal activity of the tissue in which they occur. For this assumption there is no real evidence, and, remembering the relative scarcity, the minute size, and the undoubted transitory existence of these cellular collections, it seems highly improbable that a mechanical effect of any importance can be so produced.

Marinesco has discussed the pathogenesis of myasthenia in relation to the cases of two sisters affected by the disease. He maintains that it is characterised by hyperoxygenation, which is shewn especially in connexion with voluntary movements and which results in by-products

entering the circulation and producing chemical alterations in the constitution of the musculature. The primary cause of the disease must be sought for, therefore, in some interference with the formation of anti-bodies of fatigue. In 1906 I suggested that the clinical manifestations of muscular fatigue, so characteristic of myasthenia, might possibly be explained by assuming a diminished functional activity on the part of the sarcoplasmic, as compared to the fibrillar, elements of the muscles, with the result that the fibrillar constituents, acting at a considerable disadvantage, become readily and rapidly exhausted when excited either by the will or by the faradic current. Knoblauch, in 1908, advanced a very similar view, submitting that in cases of myasthenia there is a preponderance of pale at the expense of red muscular fibres, and pointing out that the myasthenic reaction is nothing more than a normal reaction of the pale fibres unsupported by a due proportion of the red variety. Should this line of argument be strengthened by future investigation, myasthenia will be brought into interesting relationship to Thomsen's disease, in which everything points to a relative preponderance of the red or sarcoplasmic fibres at the expense of the pale or fibrillar elements.

These hypotheses, however, refer to the well-known phenomena of fatigue and do not deal with the disease as a whole. As has been already stated, the influence of pregnancy on the course of the disease provides the most important fact for the elucidation of its pathogenesis, and suggests that the fetus *in utero* is capable of providing some substance, a deficiency of which is the cause of the maternal myasthenia. Kohn's patient shewed symptoms of the disease after her fourth pregnancy, improved during her fifth pregnancy, which ended normally, but died suddenly two days later from respiratory failure. In Goldflam's case each pregnancy had a favourable influence on the disease. Sinkler's patient developed all her symptoms shortly after delivery. I owe to Dr. Head the opportunity of seeing a woman under his care who improved remarkably during pregnancy, but who had a severe relapse within a few days of the child's birth. On the other hand, several instances have been recorded in which the symptoms have not been improved, have perhaps been aggravated, during pregnancy, and Dr. Gemmell performed a successful Caesarean section on a patient of Dr. Warrington's.

Bearing in mind that the symptoms of myasthenia are not confined to the motor system, and taking into consideration the facts already mentioned, we may not be far wrong in supposing that some disturbance of glandular function is responsible for a modification of muscular activity of the nature indicated above, and for such alterations in sensibility and mentality as are occasionally met with in the victims of the disease.

**Symptoms.**—The characteristic feature of myasthenia gravis is a condition of motor impairment affecting the skeletal muscles generally, but those supplied by the cranial nerves in particular, and varying from a slight degree of exhaustibility to complete paralysis. The fact that

many of the affected muscles shew marked differences from time to time in the amount of their paresis, distinguishes the disease from most of those to which it has a superficial resemblance.

The so-called myasthenic phenomenon is demonstrated when a move-



FIG. 14. Tracing of the curve produced by faradising the biceps muscle of a healthy person; the circuit was completed at *a* and broken at *b*.

ment is repeated volitionally or when a muscle is excited by the faradic current for a certain period of time; in either case the result is a progressively weaker contraction, the diminution in power taking place

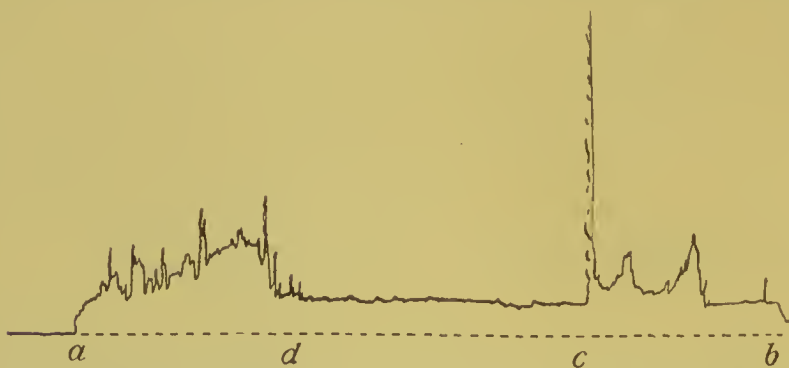


FIG. 15.—A similar tracing, using the same current, from the biceps of a myasthenic patient. At *c* the strength of the current was increased and a momentary more powerful contraction was obtained but not sustained. Although rapidly fatigued there was never complete relaxation of the muscle between *d* and *c*.

more rapidly than in healthy individuals. Moreover, a short period of rest is generally sufficient to allow the muscle to contract with as much power as it did before it had been exhausted. Three further points are important; in the first place, a muscle may be paretic or completely



paralysed for long periods of time, in which case exhaustibility is not easily demonstrated; secondly, a muscle which is easily fatigued by volitional effort may not be so readily exhausted by faradism; thirdly, a muscle which no longer responds to volitional or faradic stimulation continues to contract briskly and normally to the make and break of the continuous current.

The onset of the disease may be insidious or acute, and is not infrequently associated with vague pains, headache, and even vomiting. The paresis or fatigue is often described by the patient in the first



FIG. 16.—A myasthenic patient attempting to look up. Note the unequal ptosis, the strabismus, and the drooping of the lower jaw.

instance as a sense of weight or stiffness or numbness in the affected parts. In nearly half the cases an ocular palsy, indicated by ptosis, strabismus or diplopia, is the initial symptom, and may occasionally remain the only evidence of the disease for months or even years. Difficulties in articulation, mastication, or deglutition are among the other early phenomena, paresis of the limb or trunk muscles only rarely taking their place, although common in the later stages. The symptoms are usually bilateral but not markedly symmetrical, the corresponding muscles on either side being unequally affected more often than not.

*Muscles supplied by the Cranial Nerves.*—All forms of ocular palsy from



weakness of one external rectus to complete external ophthalmoplegia may be observed; ptosis is said to occur in about 75 per cent of the cases. Partial bilateral ptosis gives the patient a sleepy appearance and induces him to throw his occipito-frontalis muscle into action in order to assist in keeping the palpebral fissure open. When the latter muscle is also affected he will extend his head backward in the attempt to look at an object in front of him. The pupillary light reflex is rarely lost, but has more than once been noted as remarkable for its ready exhaustibility. Accommodation may be affected, but usually escapes. Jerky nystagmoid movements can often be elicited, especially when the ocular muscles have already been fatigued.

Paresis of the muscles moving the lower jaw interferes with mastica-



FIG. 17.—This photograph, which shows the smile of a myasthenic patient, illustrates two points. In the first place there is marked asymmetry. In the second place the "nasal" or sneering character of the smile can be readily seen on the left side of the face when the right half is covered. When the left half is covered a normal smile is displayed on the right side. This condition is due to deficient action of the zygomatic muscles and possibly of the risorius on the left side.

tion and articulation, the patient being obliged to support his chin with his hand in order to counteract the tendency to jaw-drop.

Of all the muscles in the body the orbicularis palpebrarum probably escapes least in this disease, and very few instances are seen in which the patient is able to close his eyes with normal strength. The other facial muscles are frequently affected to a greater or less extent, and alterations in expression, especially the nasal smile described by Sir W. Gowers, are the result. Inability to close the oral aperture may lead to the dribbling of saliva, and the power of whistling or of blowing out the cheeks is diminished or lost. Paresis of the palatal and pharyngeal muscles gives rise to a nasal voice, to regurgitation of fluids through the nose and to difficulty in deglutition; semi-solid food-stuff is generally most easily swallowed. A characteristic myasthenic reaction may be

observed in the vocal cords, and complete aphonia is occasionally met with. Movements of the tongue are often impaired, both in lateral and antero-posterior directions; this may prevent the patient from clearing his mouth of food.

All the disabilities referred to tend to increase as the attempt to repeat the movements is continued; articulation, which is clear enough to begin with, becomes unintelligible at the end of a conversation; a meal may be begun but not finished; a few lines may be read, but from increasing fatigue of the ocular muscles the patient is unable to finish the page.

*Muscles supplied by the Spinal Nerves.*—Asthenia of the muscles supporting the head is by no means rare, and the patient is obliged to recline or to use his hands to aid in keeping it in position. In the same way the implication of the trunk muscles may be sufficiently severe to prevent him altering his position in bed or maintaining the erect posture. Weakness of the respiratory musculature is a menace to life, especially in the event of any pulmonary complications, and attacks of sudden dyspnoea are among the most distressing and fatal incidents of the disease.

Any or all of the muscles of the limbs may present the myasthenic phenomena, although it is rare to find the extreme degree or permanency of paralysis which is so often present in those supplied by the cranial nerves. Speaking generally, the larger proximal muscles are more commonly affected than those of the hands and feet. The power of writing may be easily exhausted, and the legs may give way after walking short distances. The ascent of stairs is often a severe test to which to put the patient, and the risk of inducing respiratory embarrassment in bad cases contra-indicates any such attempt.

In the description of the above symptoms emphasis has been laid upon the more severe examples of disablement, but it must be remembered that very slight degrees of myasthenia are not uncommon and require careful methods of examination for their detection. When some marked ocular palsy attracts the attention of the observer the affection of other parts is not so likely to be missed as when the limbs are the only regions involved, and these only to a comparatively mild extent. There is little doubt that the exhaustibility of the musculature as a whole is unfavourably influenced by the tiring of a particular part, and that emotional or psychical influences may increase the liability to fatigue. It has frequently been noticed that the patient is at his best in the early hours of the day and becomes progressively worse as night approaches. The menstrual period exercises an adverse influence on the female cases, and extreme degrees of temperature have a bad effect in some instances. Myasthenic muscles are somewhat flabby and hypotonic, but definite evidence of atrophy is only occasionally detected. When wasting occurs, however, it may progress rapidly. The glossal and facial muscles appear to undergo atrophy more frequently than any others, but I have observed the pectorals to be severely affected in this

way in a case of long standing. Other observers have noted the same thing in the neck, the masseters, the upper arms, and the intrinsic muscles of the hands. The tongue often presents two lateral furrows due to this cause, and fibrillation of that organ is by no means uncommon.

*Electrical Reactions.*—A few words may be added to what has already been stated about the electrical reactions of myasthenia. A muscle which is severely affected may not respond at all to a faradic current of mild strength; the application of a stronger current will produce a contraction which, however, is poorly sustained. Other muscles may respond fairly well to an average current to begin with, but the contraction gradually relaxes, although the electrodes are kept in situ. This relaxation of the muscle is not as a rule a steady one; it is broken by temporary reinforcements of the contraction until it reaches a level at which it remains fairly even. The strengthening of the stimulus at this point induces a strong contraction, which again very rapidly fails. With the galvanic current the muscle shews little evidence of fatigue, although the circuit may be rapidly made and broken for a considerable period of time. Atrophic muscles may give the reaction of degeneration.

*Reflexes.*—The tendon-reflexes are usually obtained with ease, even when the muscles are flabby and paretic. On the other hand, they may be diminished or very easily exhausted by repetition in the case of muscles which are severely affected. The complete exhaustion of a muscle by faradism or volitional effort does not abolish, although it may impair, the direct excitability of the tendon. Superficial reflexes are generally preserved and the plantar response is of the flexor type.

*Sphincters.*—With the exception of one or two cases in which slight incontinence of urine was noted, the control over the sphincter vesicae and sphincter ani is unaffected in this disease.

*Sensibility.*—Aching or sharp "lightning" pains as well as migrainous headaches and various forms of neuralgia are often complained of by myasthenic patients. Numbness and other forms of paraesthesia have also been noticed in a number of cases. Objective loss is rare, but I have published a case in which relative analgesia and anaesthesia were so marked and so characteristically distributed as to suggest the possibility of their tabetic origin, especially as they were associated with pains of a lightning type and diminished tendon-jerks. Other authors have made similar observations, although the distribution and degree of sensory loss have not been so remarkable.

*Psychical Symptoms.*—Myasthenia does not appear to be associated with any special mental state if allowance is made for the natural depression produced by so disabling and distressing a disease. Instances of marked melancholia, in one case accompanied by suicidal tendencies, have been recorded (Lannois, Klippel, and Villaret; Buzzard (4)).

The course and duration of the disease vary very greatly, and thus make the prognosis in individual cases extremely difficult. Instances in which the whole duration has not exceeded a week or two and which have ended fatally can be found in the literature, and it is difficult to

recognise any essential points of difference between these cases and others which have survived a great number of years. Remissions and exacerbations are common features of the disease, if, indeed, they do not form its chief characteristic. Favourable results have been reported from time to time, but it cannot be denied that death is the usual termination, and that every case must be regarded as one of great gravity. The mild character of the symptoms during a prolonged period is no guarantee against an acute exacerbation of a dangerous and even fatal kind. Although life may be preserved for some years it is hardly ever possible for the patients to pursue their vocations, and anything like hard physical labour is out of the question. In the majority of instances death is due to failure of the respiratory musculature.

**Prognosis.**—The difficulties in forming an opinion as to the outcome of any case of myasthenia have already been mentioned, and it is impossible in the present state of our knowledge to advance any data upon which a reliable prognosis can be built. Emphasis can only be laid upon the grave and dangerous character of the disease, and attention drawn to the fact that the issue is sometimes, although rarely, favourable.

**Diagnosis.**—In the majority of cases no difficulty should be experienced in diagnosing this disease if the possibility of its presence is remembered and if its characteristics are known. The occurrence of paresis in any of the muscles supplied by the cranial nerves should arouse a suspicion of its existence and lead the medical observer to investigate most carefully the mode of its onset, the character of its course, and the nature of its physical phenomena. The chief incidence of the affection upon the ocular muscles, and the great variability in the degree of paralysis from time to time, together with the absence of marked muscular atrophy, suffice to distinguish myasthenia from ordinary bulbar paralysis. The phenomena of fatigue are much more marked than any met with in cases of hysteria or neurasthenia, and the latter conditions are more likely to wear their worst aspect in the morning and after rest than in the evenings and after exertion. Moreover, cranial nerve palsies are never hysterical in origin, and confusion can only arise in those less common cases of myasthenia in which moderate degrees of paresis and ready exhaustibility are confined to the limbs and trunk. The demonstration of the myasthenic electrical reaction is valuable as a positive sign, although its absence is never enough to exclude the disease.

The condition of the reflexes, the sensory changes, and the presence of muscular atrophy with the reaction of degeneration are enough to distinguish cases of multiple neuritis, and it is not improbable that some of the cases which have been described as post-diphtheritic chronic bulbar paralysis have, in reality, been examples of slowly progressive myasthenia.

Instances of ophthalmoplegia without any other signs of disease, and without obvious origin in some such morbid process as cerebral syphilis, afford the most difficult type of case from the point of view of



diagnosis, and necessitate patience and very careful examination before an accurate opinion can be formed. In some of these, only constant observation over a considerable period of time will determine the solution of the problem.

The myopathic and the myasthenic facies may sometimes strongly resemble one another, but further investigation of other parts should easily put any doubts at rest as to the category to which it belongs.

**Treatment.**—The general features of myasthenia gravis, and particularly the absence of any gross structural changes, lead one to hope that it may eventually be classed among the curable ailments, but the appropriate remedial measures are still to be discovered. At the present time we are obliged to be content with securing for the patient those conditions which do not aggravate his symptoms, and with giving a trial to those forms of treatment which appear to have exerted some favourable influence in isolated cases. Rest, warmth, good food, careful nursing, gentle massage, galvanism, and attention to general health meet most of the indications, and the administration of certain glandular extracts is always justifiable, if rarely successful. Some benefit has been claimed from the use of the dried extracts of the thyroid, thymus, ovary, and pituitary body, but their multiplicity affords ample evidence of their inefficacy. To the same category belong suprarenal extract and adrenalin, both of which have been tried in vain.

Even the few records of successful treatment must be regarded with some scepticism in view of the remarkable remissions forming an integral part of the natural history of the disease.

Certain symptoms have to be met by the best means we can employ for their alleviation. The danger of choking when deglutition is seriously embarrassed must be avoided by rectal feeding, the use of the stomach-tube being contra-indicated on account of the emotional disturbance and exhaustion it is apt to produce. Concentrated food of high nutritive value should be given in the early part of the day, in small quantities at a time, to those cases who are still able to swallow when at their best. The food should be semi-solid and finely minced in order to spare the muscles of mastication. Attacks of respiratory failure may sometimes be cut short by drawing the tongue forward, by performing artificial respiration, and by the administration of oxygen, but their repeated occurrence must generally be regarded as evidence that a fatal termination is not far distant. Arsenic and strychnine are probably harmless, and may improve the patient's general condition.

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## FAMILY PERIODIC PARALYSIS

By Prof. J. MICHELL CLARKE, M.D., F.R.C.P.

**Definition.**—A rare disease with marked hereditary tendency in which attacks of more or less extensive flaccid motor paralysis occur periodically, with loss of electrical excitability in the paralysed muscles and of the corresponding reflexes, but without affection of sensation or of consciousness. Between the attacks the patient is well.

**Etiology.**—The most striking feature in the etiology is the hereditary character of the disease. Thus, in the family recorded by E. W. Taylor there were 11 cases in five generations, Goldflam also found 11 cases in the

family of one of his patients on the mother's side, and Holtzapple 17 cases in four generations. The disease is generally transmitted indifferently through the father or mother, though in a few instances inheritance has been through the same sex. But, as in other diseases with a similar hereditary character, individual cases occur in which no other member of the family has been affected. The families subject to periodic paralysis are in other respects healthy, and do not shew any degenerative tendencies or evidence of other nervous diseases. Exception must, however, be made in this respect with regard to the family reported by Holtzapple, in which there was a remarkable association with sick headache.

No cause for the original appearance of the disease is known; it has not any connexion with malaria or the other specific fevers. In one family the patient first affected had his initial attack after running violently.

With regard to the exciting causes of the attacks themselves, the most constant is excessive or violent exertion; this in most cases induces an attack, which, however, does not supervene immediately, but after an interval of rest. In a few instances the attack has appeared to be brought on by excitement or emotional disturbance, and in others it has followed upon an accident, such as a severe sprain or a fall into cold water. Over-indulgence in rich, especially sweet, foods has been regarded as the exciting cause in several instances, such indulgence being regularly followed by an attack of paralysis. This was noticeable in several members of the family recorded by Holtzapple, in some of whom an attack was preceded by voracious appetite. The large majority of attacks, however, occur without any assignable cause.

**Pathology.**—Of the pathological conditions underlying the disease little is known. Necropsies in two of Holtzapple's cases gave negative results (Winternitz). The first point for consideration is the seat of the origin of the paralysis. This must be placed in the muscles themselves, for the loss of direct irritability to electrical and mechanical stimulation during the paralysis precludes the peripheral nerves or even the neuro-muscular junctions as the seat of lesion. Some support for this is given by the changes found in excised portions of muscle by Goldham, Crafts, and Singer, which consisted of marked fissuring and vacuolation with increased separation of the fibres. Although, as Singer points out, these changes may partly be artifacts, they at any rate shew an abnormal sensitiveness to ordinary methods of hardening and staining. Since many of the attacks of paralysis depend on previous over-exertion, it has been supposed that an abnormal tendency to accumulation of the waste products of muscular action causes the paralysis, but the concomitant loss of response to volitional, and to direct and indirect faradic and galvanic stimulation, is not seen in the paralysis of exhausted muscles (E. F. Buzzard). Although the action of some toxin is an obvious suggestion and is supported by the temporary character of the paralysis, the frequent occurrence of sweats, and the not very infrequent history of

gastric or intestinal disturbance, the existence of such a toxin has not been established. Crafts stated that he isolated a toxin from the faeces, which produced in forty-eight hours paralysis in guinea-pigs, but this observation has not been confirmed. Dr. Goodbody and others have found the toxicity of the urine increased during the paralytic attacks, but the cause of this has not been determined. The objection that if such a toxin be present the muscles supplied by the cranial nerves could hardly escape is not perhaps insurmountable. Lastly, the marked hereditary character of the disease and its frequent onset about puberty must be borne in mind. It is possible that this indicates a primary defect of development in the muscles, or of the biochemical constitution of the muscular machine. In this connexion, it would be interesting to obtain further information on Mitchell, Flexner, and Edsall's observation of a very low creatinine excretion for days preceding and during an attack, followed by a high rise after it, independent of the food taken, and also of the nitrogenous excretion. According to Dr. Spriggs by far the greater part, if not all, of the endogenous creatinine in the urine is derived from muscular tissue, being a product of the internal structural metabolism of muscle and not of its contraction.

**Signs and Symptoms.**—Both sexes are affected. The age of onset has been as early as two years, "as soon as the patients were able to move about" (E. F. Buzzard), and as late as thirty-five; but in the large majority it is at or about the time of puberty. The frequency of the attacks is extremely variable: they may occur daily, even more than once a day, or there may be an interval of months. The history commonly shews that the attacks in the early stages come on at fairly long intervals, then become more frequent between the ages of twenty and forty, and subsequently appear at longer and more irregular intervals. The duration varies from a few hours to eight days, the average being from twelve to twenty-four or thirty-six hours. Occasionally there is an interval, or intervals, of partial recovery in the course of an attack, after which the symptoms again appear.

The time of onset in the majority of the attacks is at night, often during sleep, so that the patient, who has gone to bed in good health, wakes up more or less paralysed. The onset is generally gradual, but may be abrupt.

Prodromal symptoms are most often absent. Among those occasionally described are: a sense of weakness, or a "heavy, sleepy, tired" feeling, numbness of the limbs or formication (rarely), a sensation resembling that produced by faradisation (E. F. Buzzard), or voracious appetite. In nocturnal attacks these may be felt before the patient goes to bed. The attacks, especially the milder ones, can sometimes be "walked off," but in such cases it is almost invariably found that they are merely postponed.

The characteristic feature of the attack is a gradually extending motor paralysis, which begins in the legs, and spreads to the muscles of the trunk, arms, and neck until, in the fully developed form the patient

lies helplessly in bed, unable to move or to turn his head. The paralysis affects the proximal before the distal parts of the limbs. Speech and deglutition, the muscles of the face, eyes, and tongue, the diaphragm, and the sphincters are unaffected. In severe cases the intercostals are paralysed; the patient cannot sneeze, cough, or breathe deeply, and may have difficulty in swallowing, and the breathing may be laboured. Bilateral partial ptosis has been observed, but the muscles supplied by the cranial nerves usually escape. The paralysed muscles do not respond to direct or indirect stimulation by the faradic or galvanic current, and in those partially paralysed this loss of electrical excitability is proportional to the degree of paralysis; there is no polar change nor reaction of degeneration. Idiomuscular irritability is lost or diminished. The deep and often the superficial reflexes are absent in the affected parts. Sensation is unaltered, and as a rule there are no subjective sensory disturbances, but occasionally numbness, formication, or a sense of weariness makes the patient ask for frequent changes of posture.

Consciousness is entirely unaffected. Generally speaking, there is no desire for micturition, unless the bladder becomes over-distended, nor for defecation during the attack, even for as long as forty-eight hours. Sometimes micturition is difficult or impossible; in one case there was incontinence of urine. The circulation is, as a rule, well maintained, but in severe attacks the pulse may be weak and irregular; dilatation of the heart (first observed by Oppenheim) not infrequently occurs during the attack, and this may be accompanied by a systolic murmur or a modified first sound at the apex, and by accentuation of the pulmonary second sound.

In milder attacks the paralysis may be extensive but not absolute, or the legs, arms, or neck only may be involved, or the patient may be paralysed on one side and paretic on the other: in such cases, the legs are generally most affected, the proximal more than the distal parts, and the flexor more than the extensor muscles.

Further, the patient may present pallor of the complexion, decline food during the attack, and occasionally complain of thirst; the tongue may be thickly coated, the breath heavy, there may be profuse sweats, and congestion of the conjunctiva and of the mucous membrane of the respiratory tract with accumulation of mucus in the bronchial tubes (Holtzapple). One case had slight spasm and pain in certain muscles (Schlesinger).

*Urine.*—The quantity is diminished during the attacks, and the total nitrogen, urea, sulphates, and uric acid have been found to be deficient. Holtzapple, in the affected members of his family, observed a persistent and marked diminution in the average quantity of urea eliminated, most pronounced in the worst sufferers; there was no increase in indican. Crafts found an increase of xanthine bases and of ethereal sulphates during the attack. Taylor also notes the deficient protein metabolism. A trace of albumin is very rarely present.



*Blood.*—A moderate lymphocytosis has been described in a few cases, but there are no changes of importance.

The attacks pass off gradually, as a rule, but the decline may be rapid. When recovery begins there is rarely a relapse; the muscles recover in the reverse order of their affection, and concurrently with recovery of voluntary power the reflex and electrical excitability are regained. Occasionally vomiting or a loose action of the bowels attends recovery. In a few hours the patient may be well and able to resume the ordinary duties of life.

Some patients suffer from mild attacks in which there is some paresis, stiffness, or slight ataxia of movement, often evinced by some peculiarity of gait, or instability.

In the intervals, the patients as a rule appear quite normal and without any sign of disease in the nervous or muscular systems. Goldflam, however, found in two brothers alterations in the electrical reactions, namely, partial reaction of degeneration and slow response to stimulation associated with rapid fatigue. Oppenheim, in one patient, observed a slight atrophy of those muscles which had the poorest electrical reactions between the attacks (Taylor). In Putnam's case the attacks began in the dorsal flexors of the feet, and these muscles were readily fatigued by gymnastic exercises.

*Diagnosis.*—In a characteristic case the symptoms are so pathognomonic, in fact so unique, that if an attack be seen, difficulty of diagnosis could hardly arise. Even if the attacks were not actually observed, the description of recurring, almost complete, paralysis, lasting some hours or days, and unattended by any affection of sensation or of consciousness, and followed each time by complete recovery, together with the ascertained normal condition of the patient in an interval, should render diagnosis easy. In either event, a history of other cases in the family would greatly aid it, although the occurrence of the disease without familial tendency must be borne in mind.

Brief mention may be made of cases which present symptoms of periodic paralysis but do not correspond in other respects to the description given above. Thus, Donath described a case in which the attacks appeared after an injury to the foot, and in which there was occasional delirium; in Bornstein's case the attacks occurred in a man of fifty-six and were accompanied by mental depression and marked vasomotor disturbances; and Bernhardt's cases, father and son, in whom there was hypertrophy of certain muscles followed later by atrophy of some of them, present important differences from the ordinary type. Again, Kramer's case is of interest in view of the resemblance which the muscular symptoms of periodic paralysis may bear to those of myasthenia gravis. The onset was late, at sixty years of age; the paralytic attacks were always accompanied by pronounced myasthenic symptoms, and also by glycosuria. Both the myasthenic symptoms and the glycosuria disappeared in the intervals, the latter gradually. The paralytic attacks could be produced almost certainly by increasing the amount of protein

and carbohydrate in the diet, so as to cause the appearance of sugar in the urine. (*Vide* also art. "Recurrent Paralysis," Vol. VIII.)

**Course and Prognosis.**—It has been said that as age advances, the attacks generally become less frequent and less severe. The prognosis as to life is usually good; indeed until 1905, when Holtzapple published the account of a remarkable family, it would have been said to be absolutely favourable, for the only fatal case was that published by Schachnowitsch in 1882, which was regarded by many as a doubtful one. But of the seventeen patients in the family recorded by Holtzapple six died in attacks, three of the latter being brothers. The age at death ranged from twenty-five to fifty-four years. The fatal attack witnessed by Holtzapple was characterised by accumulation of mucus in the bronchial tubes, cyanosis, and dilatation of the heart, death being due to cardiac failure. The occurrence of a death from this cause in a family would probably justify a guarded prognosis in another member. Of bad omen would be embarrassment of respiration and marked cardiac dilatation in the attacks. It would naturally be anticipated that the repeated occurrence of dilatation of the left ventricle should in time lead to permanent mitral insufficiency, but I can find no evidence on this point. In one of Holtzapple's patients, weakness of the legs began at the age of fifty-two, followed at seventy by paraplegia with absent reflexes in the legs, but without any alteration of sensation or of the sphincters.

**Treatment** is unsatisfactory, and most observers have found electricity and massage useless. Otto and Darconrt, however, state that the attack is shortened by faradisation, and Oddo and Andibert recommend treatment of attacks by passive movements and faradisation. Holtzapple advises half a dram of bromide of potassium with one or two grains of caffeine, repeated in one or two hours, and says that although it does not cure, it has a very decidedly abortive influence and hastens improvement when taken during a paroxysm. In Singer's case the administration of mild diuretics in the form of imperial drink, digitalis, and acetate of potassium diminished the frequency of the attacks, and Mitchell, Flexner, and Edsall in two cases found that citrate of potassium, and in less degree bromide, were of service. From what has been said above, it is obvious that over-exertion, late hours, excitement, and dietetic excesses, especially of sweet foods, should be avoided, and that every care should be taken to maintain the general health.

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J. M. C.

## NEURITIC TYPE OF PROGRESSIVE MUSCULAR ATROPHY

### *Peroneal type (Chareot-Marie-Tooth).*

By FREDERICK E. BATTEN, M.D., F.R.C.P.

**Introduction.**—This form of progressive muscular atrophy lies midway between the myopathic and the myelopathic affections; in its clinical aspects it is closely allied to the myopathies, but anatomically a definite change in the spinal cord has been established. The characteristic features of this affection are: A slowly progressive muscular atrophy with weakness, starting usually in the peroneal and anterior tibial muscles, spreading gradually to the other muscles, so that all the muscles below the knee are wasted, whereas the thighs remain in moderately good condition. Following the atrophy of the legs there is wasting of the small muscles of the hands and forearms. There is some alteration of sensation over the periphery of the legs, and vasomotor disturbances are common.

**History.**—This form was first described by Chareot and Marie in 1886, and in the same year by Dr. Tooth, who collected the recorded cases, among which were the accounts of 4 necropsies by Virchow, Oppenheim, and Friedreich; in two of these spinal changes were absent, whilst in the other two there were changes in the posterior columns.

Numerous cases have since been described. Dr. Herringham has given an account of a family in which the affection occurred in twenty members and could be traced for five generations. Hoffmann, Siemerling, and Sainton have more recently investigated cases pathologically.

**Etiology.** *Age.*—The disease usually commences during the first decade, but may appear in the second or third decades of life.

**Heredity.**—The disease is transmitted both by males and females, and both sexes are attacked. But in the family reported by Dr. Herringham males only were affected, though the disease was transmitted by the

females, following closely the hereditary features noticed in colour-blindness. In a considerable number of cases no evidence of heredity can be obtained. In some instances the onset has directly followed measles (Ormerod, Batten).

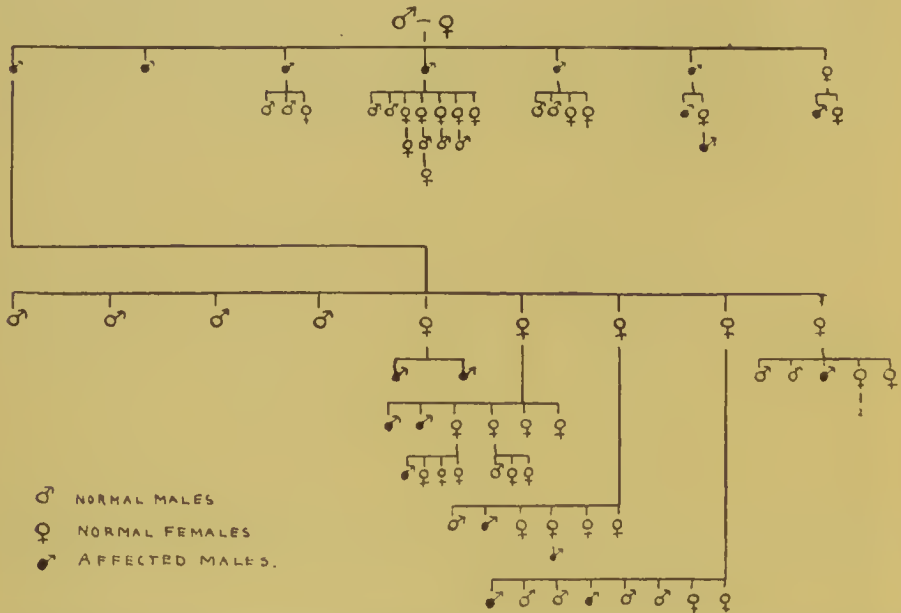


FIG. 18.—Pedigree of muscular atrophy of peroneal type. The usual signs are used to indicate males and females. The affected males are marked black. There are no affected females. It is to be noted, however, that the unaffected females bear affected males—whereas the affected males have normal children. (Herringham.)

**Morbid Anatomy.**—There is some confusion with regard to the pathology, owing to the fact that several different conditions have been included under the neuritic muscular atrophy of Charcot, Marie, and Tooth. Sainton carefully reviewed the subject and excluded many of the doubtful cases. In his case the following changes were found. The cord shewed sclerosis of the posterior columns, especially of the columns of Burdach, slight degeneration of both pyramidal tracts, alteration of the cells of Clarke's column, and atrophy of the cells of the anterior horns. There was slight degeneration of the intramuscular nerves, slight sclerosis of the nerves of the forearm and leg, this being well marked in the peroneal nerves only. The larger nerves, such as the sciatic, were normal. The muscular fibres were atrophied and in some places had completely disappeared, connective tissue being substituted. Almost the same changes were found in Siemerling's case, the degeneration being most advanced in the postero-median columns and in the lumbar and lower dorsal regions of the cord. The change in the muscles was that of simple atrophy of the muscle-fibres, and not such as is met with in the myopathies.

**Symptoms.**—The disease starts in the lower extremity, with weakness



and wasting of the peronei which give rise to foot-drop and inversion of the foot, so that the child walks on the outer side of the foot. The atrophy progresses and involves all the muscles below the knee, but the patient is usually well able to get about as the muscles of the thigh remain in good condition. The distribution of the atrophy gives the leg

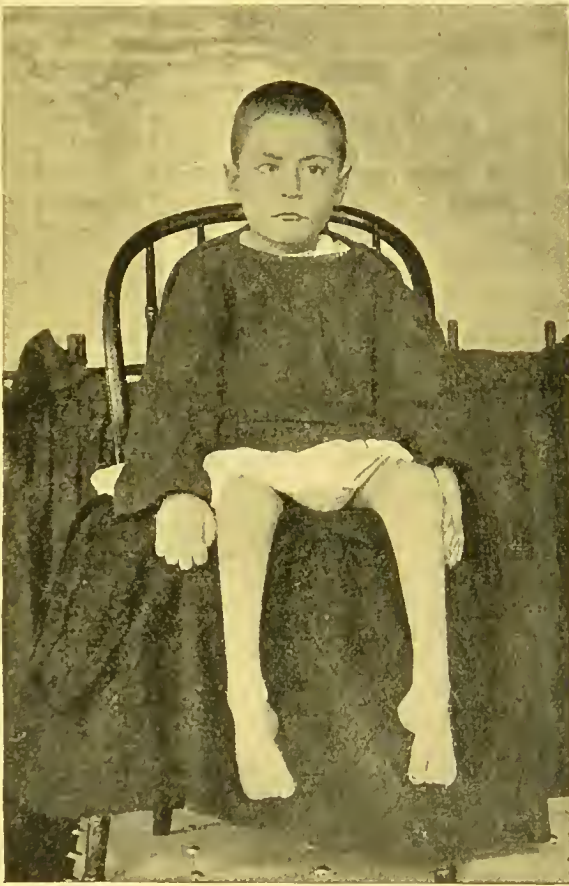


FIG. 12.—Photograph of a boy, aged seven, with peroneal atrophy. The legs shew the wasted condition of the muscles below the knees. The position of the hands is characteristic, although the atrophy is not well shewn. (*Trans. Clin. Soc.*, 1899, xxxii. 239.)

a curious bottle-shaped appearance, the lower portion of the leg representing the neck of the bottle.

Chareot pointed out that it is the distal portion of a muscle which is first affected. Fibrillar tremors have been observed in the affected muscles. In association with the atrophy of the muscles, there is some loss of tactile sensation, and loss of muscular sense has also been observed. The muscles and nerve-trunks are not tender. Vasomotor disturbances are sometimes present, generally in the form of cyanosis, but sometimes there is a marble-white appearance of the extremities. The muscles lose the power of contracting to mechanical stimuli, and

there is a diminished reaction to faradism and galvanism, but a true reaction of degeneration is seldom observed. The condition is nearly always symmetrical, although exceptions to this rule occur (Herringham, Ormerod).

The ankle-jerks are usually lost at an early period, and it is difficult to obtain a plantar response. The knee-jerks remain active, and there is very little tendency for them to disappear, as the vastus internus muscle remains in good condition. The sphincters and trunk muscles are not affected. After the atrophy of the legs has been present for one to four years, wasting of the small muscles of the hands is noticed; this gives rise to a typical claw-hand, the two terminal phalanges being flexed. The disease may affect the extensors and flexors of the wrist; the atrophy, as in the legs, falls on the most distal muscles and the distal portion of the muscles. The degree of incapacity to which this affection gives rise varies very greatly. Some patients are able to follow their usual occupation for years; walking is their main difficulty, and this they surmount by riding a bicycle, which they are able to do perfectly well. The mental condition is good.

The diagnosis of a characteristic case is not difficult as a rule. The slow onset, the character of the weakness and wasting, the absence of pain, and the symmetry of the affection are the points on which most stress would be placed.

*Acute poliomyelitis* is rarely so symmetrical as this disease, and further, it is not progressive. *Multiple neuritis* might be confused with it; but the presence of pain and tenderness in the muscles, the more general affection of the muscles, and the greater sensory disturbances would distinguish ordinary neuritis from peroneal muscular atrophy.

To a *progressive muscular atrophy* of the motor neurons the disease bears great resemblance; but it differs in its course, and in the age and mode of onset from the common type of that affection, which starts in the hands and produces a spastic condition of the lower limbs.

The *muscular dystrophies*, especially the "distal" type, and peroneal muscular atrophy are so much alike that, as Spiller has pointed out, it is sometimes impossible to arrive at a correct diagnosis from clinical examination alone.

**Prognosis.**—Though progressive, the disease advances so slowly that many patients are able to pursue their ordinary work for years. The acute specific fevers accentuate the disease, and sometimes call forth its first manifestation.

**Treatment.**—No treatment is known to have any effect in arresting the disease. Mechanical support for the foot-drop will often assist the patients very considerably in walking.

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# TROPHONEUROSES

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RAYNAUD'S DISEASE.

ERYTHROMELALGIA.

FACIAL HEMIATROPHY AND  
HEMIHYPERTROPHY.



## THE TROPHONEUROSES

By H. G. TURNEY, M.D., F.R.C.P.

**Introduction.**—The term trophoneurosis, which is now generally accepted in clinical medicine and pathology, includes the double statement, that on the one hand the normal nutrition of the tissues is controlled by the nervous system, and on the other that errors in this control or its abolition are followed by recognisable results. At first sight the statement that the nervous system controls nutrition appears suspiciously like a truism, and yet few questions in physiology have proved more difficult of solution. A large amount of research has been devoted to the subject with results which, valuable as they have been in many other respects, have not yet placed beyond dispute the existence even of nervous control, far less the manner in which it is exerted. The difficulty depends upon two fundamental factors. The first of these is that the lowlier tissues, in spite of a progressive specialisation and centralisation in the course of development, have maintained a very considerable share of their original autonomy, which suffices to carry them through the average exigencies of life in independence. Nervous control, in fact, is to be regarded as rather of the nature of an ill-defined suzerainty than as an absolute government. Moreover, to carry the analogy still further, the interference of the suzerain will be apparent in different degree according as the situation of any particular territory exposes it to more or less severe strain; thus, the severance from central control which may pass unobserved in the hand may induce nutritive disturbance in the foot. Failure to recognise this fundamental point has been responsible for much of the dispute as to what should or should not be regarded as a true trophoneurosis. To demand, as is often done, that it should invariably follow the nervous lesion is in the last degree unreasonable. The second difficulty is closely allied to the first, but not identical with it. It depends upon the fact that it is almost impossible to reproduce experimentally the conditions which are found effective in human pathology. However carefully the experiment may be planned, it can hardly annul nervous control without at the same time producing either paralysis or anaesthesia, and so altering in other respects the relations of the limb to its environment. If paralysis is produced, the tissues

lose the specific stimulus for their nutrition, beside which every other factor is insignificant. Or, on the other hand, motor power may be left, but sensation be abolished; and this brings with it a fresh train of dangers such as appear after removal of the Gasserian ganglion, and in consequence of which it is even a matter of doubt if this structure has the trophic influence over the eyeball which has always been attributed to it. It is hardly surprising, therefore, that experimental science has told us little about the nervous control over nutrition, and that its professors are inclined to adopt an attitude of more or less pronounced scepticism towards it.

But before proceeding to a description of the clinical manifestations of trophoneurotic action, it is necessary to describe in as few words as possible the machinery by which, so far as we know it, normal nutrition is maintained. For our present purpose this may be taken to be the vasomotor mechanism. Trophic nerves may exist, but this hypothesis need be discussed only if vasomotor action prove obviously inadequate to account for the facts of nutrition.

*Physiological Considerations.*—The vasomotor mechanism may be considered under two headings: the one includes the larger vessels, particularly the arterioles; the other those of capillary size.

(a) *Arterial Vasomotor Mechanism.*—Control of the calibre of the arteries by means of vasomotor nerves is a matter of such familiar knowledge that no detailed description is called for. Suffice it to say that vasomotor nerves are of two kinds, vaso-constrictor and vaso-dilator respectively. The former are in constant action, and are responsible for the permanent state of semi-contraction which constitutes arterial tone. They can, however, be replaced by local mechanisms, and are themselves controlled by higher centres in the spinal cord and brain.

Though our knowledge of the vaso-dilators is less complete, there is no reason to suppose that their functions are of less importance. Until recently it was believed that vaso-dilator impulses, unlike those for vaso-constriction, did not play any continuous part in the maintenance of vascular tone, but a research carried out by Dr. Bayliss (3) makes it more than probable that vascular tone is the product of both kinds of activity—dilatation as much as constriction. The most important observation of recent years is that of Bayliss (4), which proved that the course of dilator fibres to the hind limb is by the posterior nerve-roots; and not only this, but that these *efferent* vasomotor impulses travel in all probability by an *afferent* nerve, the nutrient centre for which is in the posterior spinal ganglion. This discovery clears up some at least of the difficulties met with in correlating vasomotor action with certain trophic effects. This statement applies to clinical observation only, for, speaking broadly, every attempt to produce changes in nutrition by vasomotor action has hitherto met with failure.

(b) *The Capillary Mechanism.*—In entering upon the consideration of the capillary system there is a temptation to regard these small vessels as mere miniatures of the large, to picture them as bearing the same



relation to the artery that the rivulet does to the river. Such a conception would be a very inadequate representation of the truth. Up to a certain point, it is true, artery and capillary alike have a common function, that of transport, and this may be considered first. The means by which the artery becomes a perfect instrument for this purpose have just been summarised, and we may now consider how far the capillary is possessed of similar powers of adaptation.

(i.) The changes in its calibre are obvious, and on the whole tend to occur at the same time and in the same direction as those in the supplying artery. But this is by no means always the case; even when the capillary follows the lead of the larger vessel, it may do so only after a considerable interval, and it may never do so at all. It is clear, therefore, that these changes do not follow as a mechanical result of the expansion or contraction of the artery, but are in response to some independent, even if coincident, stimulus. Evidence is accumulating that the stimulus for this capillary reaction consists in the presence of the products of tissue metabolism; in default of this neither arterial dilatation nor venous obstruction are effective, as has been shewn experimentally (Samuel, Bier, and Lazarus-Barlow). How far the calibre of the capillaries beyond this local reaction is under the control of the nervous system is not yet absolutely assured, but some recorded observations (Lapinsky (28)) demonstrate a vasomotor control analogous to that over the arteries, the capillary endothelium altering its shape and swelling up so as to narrow the lumen of the vessel when the nerve is stimulated. Such a reaction should not be taken as in any way excluding a direct response on the part of the capillary to the chemical call of the tissues. From the present point of view the power of the capillary to vary its calibre is of relatively subordinate importance. It is a power which it shares with the larger vessels, as it shares their duty of transport. But, regarding the blood as the vehicle of nutrition, it has in the capillary arrived at its destination—the tissues—and the problem is not so much one of transport as of distribution, which involves the passage of nutritive material through its walls.

(ii.) Permeability.—It is in response to this new necessity that the capillary manifests a property henceforth to be called permeability, by which its contents, both solid and fluid, are able to pass through its wall into the lymph-spaces which at once separate and connect the vessels and the tissues. The secret of nutrition lies in the due ordering of this transit. Into the passage of the corpuscular elements of the blood there is no need to enter; it is universally recognised as a vital act on the part of the leucocytes with the co-operation of the capillary endothelium, and every step of the process may be watched under the microscope; but the passage of the fluid, which once outside the vessel we know as lymph, is a more difficult question. In a state of health the production of lymph is so regulated that every tissue receives its supply of protein and other material in quantity and quality perfectly adapted to its needs; excretory substances are received and carried off or absorbed into the

veins; at the same time the amount of fluid is subject to constant variation in accordance with changes in the blood circulation, and with all this, the net quantity of tissue fluid—the balance between production and absorption—remains in stable though mobile equilibrium. How is this regulation maintained?

Without joining in the controversy about the mechanism of lymph-production (*vide* Art. "Oedema," Vol. IV. Part I. p. 510), it may be stated that it turns upon the part played by the capillary wall. Does this act as a living secreting tissue or as a mechanical filter? Prof. Starling at the head of one school, while not denying the possibility that there may be some activity of a secretory nature, finds nothing that is not explicable by the physical processes of filtration, diffusion, and osmosis called into action by variations in blood-pressure and composition on the one hand, and on the other a fixed degree of permeability on the part of each capillary territory. The variations which are acknowledged to occur in morbid states such as inflammation and renal disease are attributed to injury to the vessel-wall, which renders it less perfect as a filter.

According to the opposing school (Lazarus-Barlow, Asher, Hamburger, Carlson) the capillary wall should be regarded as a true organ of nutrition, and its permeability as a variable quality governed by the nutritive or secretory demands of the tissues, which are conveyed by means of metabolic products acting either directly as hormones or indirectly by secretory or trophic nerves. In the following pages clinical evidence will be adduced to shew that the permeability of the capillary wall is a variable quality which is under the influence of the nervous system, and more particularly of the vasomotor nerves or centres.

### TROPHONEUROSES OF THE SOFT PARTS

It is proposed to group the various clinical types of trophism under three main headings (and a supplementary one), which correspond roughly to the physiological outlines just laid down. (1) Those which are associated with changes in the calibre of the vessels, whether large or small, *hyperaemias* and *ischaemias*. It has already been pointed out that alterations in the calibre of the capillaries do not necessarily coincide with those in the large vessels, but it is not possible to separate these clinically. (2) Those which depend upon changes in the permeability of the vessel-wall apart from changes in calibre. This group corresponds generally to the class of trophoedemas. (3) Those which shew changes in nutrition apart from either of the above factors—pure hyperplasias and hypoplasias. (4) The complicated trophoneuroses—destructive lesions in which a neurotrophic element is present but is confused by infection and other complications.

I. NEUROTROPHIC AFFECTIONS WITH ALTERATIONS OF VASCULAR CALIBRE. (*Vide* Art. "Raynaud's Disease," p. 120.)—(A.) **Hyperaemias.** (a) *Glossy skin*.—The condition known as "glossy skin" claims the first

place, if only because the modern study of the trophoneuroses was inaugurated in the descriptions of Sir J. Paget in 1864 and Weir Mitchell in 1868. Apart from its historic importance the lesion is highly characteristic. The cases on which Weir Mitchell based his description were due to gunshot injuries of the brachial plexus, and occurred in the American Civil War. Paget's original description (quoted by Weir Mitchell) is in the following words: "Glossy fingers appear to be a sign of peculiarly impaired nutrition and circulation due to injury of the nerves. In well-marked cases the fingers which are affected are usually tapering, smooth, hairless, almost void of wrinkles, glossy, pink or ruddy, or blotched as if with permanent chilblains. They are commonly also very painful, especially on motion, and pain often extends from them up the arm. In most of the cases this condition of the fingers is attended with very distinct neuralgia, both in them and in the whole arm." The only criticism suggested by this description is that it gives an inadequate idea of the suffering which this really terrible condition involves, though this comes out clearly enough in Weir Mitchell's account of the individual cases. In addition to the features mentioned, the affected area is peculiarly prone to the development of vesicles which may appear spontaneously and form the starting-point of ulcers. The skin sweats profusely, and the nails share in the changes in the other tissues. They are thin, with the blue colour shewing through, and are curved over the wasted tip of the finger. The hyperaesthesia may be so great as to make inspection the only method of investigation possible; otherwise it is found that epicritic sensation is abolished. It will be noted that the nerve-lesion is always a partial one, and, in fact, the moment the injured nerve is completely divided the suffering ceases. If relief be delayed, there is a very special tendency towards the development of adhesions about tendon-sheaths and joints which may make the restoration of conduction to the nerves of little avail. Characteristic instances were met with amongst our troops in the Boer War, one of which has been recorded in detail by Dr. Head (20). The condition may also occur as a sequel to a phlegmonous inflammation in the vicinity of a nerve-trunk or as an incident in non-traumatic spinal disease (Weir Mitchell (59), Pospelow). The symptom-group is particularly interesting, as it seems clearly to be due to nerve irritation. That the vaso-dilators are specially involved is probable in view of the hyperaemic condition of the skin and the profuse sweating over the parts affected. Dr. Head's patient was convinced that his nails grew more quickly on the affected side, and, as Dr. Head points out, his belief was supported by the contrast which they offered to the condition found when growth is undoubtedly at a standstill. In the one case both skin and nails are thin and translucent, in the other opaque and heaped up with layers of epithelium. Dr. Head found the one condition replaced by the other in his case of "glossy skin" five days after the nerve had been completely divided for relief of pain.

(b) *Herpes zoster*, upon the pathogeny of which so much light has been thrown by the researches of Dr. Head (21), must be mentioned here as



the clearest example of irritative neurotrophic lesion with hyperaemia closely analogous to the above. The vesicles and oedema shew affection of the permeability of the vessel as well; but this will be considered in a later section. The ganglion on the posterior root is proved to be the seat of the primary disturbance (*vide* p. 476).

(c) *Neuropathic Keratitis*.—The keratitis which frequently follows removal of the Gasserian ganglion and results commonly in the destruction of the eye should be classed among neurotrophic lesions, although its essential characters are obscured by the inflammation due to local conditions. Even with the most anxious care this sequel to operations on the ganglion cannot always be averted. With rare exceptions it occurs within a short period of the operation, and that period once passed, the patient is practically safe, although the anaesthesia persists (41). It may occur even when corneal sensibility is retained or replaced by hyperaesthesia. The data point strongly in favour of the view that the nerve condition is one of irritation, and the effects on the eye, as seen in the early intense hyperaemia and tendency to vesiculation, are closely comparable to glossy skin and herpes. An organism has recently been described (Davies and Hall) as the agent responsible for neuropathic keratitis, but it can hardly be regarded as the true *causa causans*.

(B.) *Ischaemic Type*.—(a) *Symmetrical gangrene* constitutes the commonest trophic neurosis attributable to vasomotor disturbance, particularly to the form known as Raynaud's disease (*vide* p. 126). It may follow either the syncopal or the asphyxial form, and is nearly always of the dry variety. As a rule it causes the loss of the tips only of one or two fingers, or of the ear, but in some recorded cases a great part of an extremity has necrosed *en masse*. These, however, are very rare, and it is doubtful if they should be ranked as pure neuroses, as they are generally asymmetrical and in other respects atypical. The vasomotor instability which forms such a prominent feature of organic arterial disease may very closely simulate the pure neurosis, though on the other hand it should be remembered that prolonged disturbance of innervation will itself bring about changes in the wall of the vessel (28, 29). Where the patients are advanced in years, or are even arrived at middle age, the presumption must always be on the side of arterial disease.

(b) *Multiple neurotic gangrene* (9, 42) has many points of similarity with the condition just described, but lacks its limitation to the periphery and its symmetry. Patches of skin in any part of the body may become gangrenous, and the process may be repeated over many years without the appearance of constitutional symptoms.

(c) *Herpes zoster gangraenosus hystericus* (Kaposi) is a remarkable affection, similar to the above, but distributed according to segmental areas.

The Raynaud symptom-group, with gangrene as an epiphenomenon, is occasionally found in syringomyelia (54), and more rarely in association with tabes, tumours of the spinal cord, and peripheral neuritis.

## II. TROPHIC LESIONS WHICH DEPEND UPON CHANGES IN THE VASO-



PERMEABILITY FACTOR—THE TROPHOEDEMAS.—Before considering the clinical evidence for the occurrence of oedema under nervous control, it must be borne in mind that the function of lymph-formation or vaso-permeability is highly sensitive to influences other than nervous. In the first place it is sensitive to changes in the constitution of the blood, which would be otherwise unrevealed; thus a reduction of the calcium-content, a condition which can hardly even be regarded as pathological, may cause the form of exudation which is known clinically as urticaria. The presence of endogenous or other toxins, as in renal disease, or the existence of an inflammatory focus, may induce an oedema which will spread over a large area, or even over the whole body. Secondly, variations in blood-pressure must also be taken into account, though it is a matter of doubt if an increase of blood-pressure *per se* is an effective cause of oedema. In human pathology, at all events, it hardly ever occurs in the absence of stagnation, which must affect the nutrition of the capillary wall. It is clear that the diagnosis of a neuropathic oedema calls for special caution, and can be regarded as established only when these complicating conditions are excluded. Oedema has been observed in connexion with lesions at every level of the nervous system, as is borne out by the following list, which might be lengthened indefinitely.

Oedema following *lesions of the peripheral nerves* has been noted on numerous occasions as, for example, associated with perforating ulcer in a case of injury to the sciatic nerve reported by Rochet (cf. Lapinsky, 29). Oedema is the most characteristic feature of beriberi; where it occurs in the later stages of the disease, there may be some doubt as to the exact mode of production; but when it is found early, as is often the case, it must be accepted as a true trophoedema. Lesions of the posterior spinal ganglion, as revealed by herpes zoster, constantly cause oedema of a special type in the form of vesicles, and, besides the vesicles, there is often a generalised oedema over the affected area (50).

Among lesions of the spinal cord, syringomyelia is, as might be expected, the most fruitful. Schlesinger states that one of the commonest cutaneous manifestations is an eruption of blisters either of the herpetic or pemphigoid type. In the same disease an oedema has been repeatedly observed, limited to the part of the body affected by the nervous derangement, and unaccompanied by any signs of cardiac or renal disease, or even of a local vasomotor reaction. It may appear and disappear with great rapidity, and tends to occur in the neighbourhood of joints particularly, but not only when these are the seat of a dystrophy (Schlesinger). In *tuberculosis dorsalis* the same phenomenon occurs, and with a similar distribution—an area to which lightning pains are referred, being not uncommonly the seat of a neuropathic oedema. In a case of *paraplegia dolorosa* I recently saw the almost sudden appearance of an extreme degree of oedema over the paralysed parts, with trophic changes in the skin, and without any indication of circulatory interference. The patient had been confined to bed only a few days, and there was no impairment of the general nutrition.

Oedema may result from psychical causes alone. Numerous instances are recorded of the production of exudation and vesiculation by hypnotic suggestion; and though many of these will not stand criticism, there is a residuum above suspicion. For example, Kohnstamm described a case in which the process took place before his eyes; and other examples of more or less cogency may be found in works on hypnotism.

Beyond these types with clearly defined neurogenic associations is the far larger class of oedemas in which the origin in the nervous system is arrived at rather by a summation of probabilities than by direct proof. The evidence is very similar to that which in the opinion of the vast majority of observers entitles the vasomotor neuroses to their name; but, just as with the vasomotor neuroses, individual cases are met with in which it is impossible to say whether they should be classed amongst diseases of the vascular or of the nervous systems, so is it with the oedemas. On the one side they shade off imperceptibly into the vasomotor neuroses, and on the other into the dermatoses. Often oedema occurs as an element in a vasomotor neurosis; but its significance is missed, because it is generally ignored, except as a mere detail of the vasomotor disturbance; that is, of the alteration in calibre of the vessels and consequent increase of capillary pressure. That this is not an adequate explanation is shewn by the fact that the oedema may not only follow the asphyxial condition but may precede it, and sometimes occurs quite independently of any visible circulatory change (Raynaud).

The following clinical types may be recognised, it being remembered that they are clinical types only, and that the lines of demarcation are often overlapped. (1) Angioneurotic oedema, in which the oedema is associated with local nervous symptoms. There are two sub-groups: (a) the blue oedema of Charcot, with vasomotor phenomena; (b) hysterical oedema, without vasomotor phenomena, but with disturbance of the vaso-permeability function.

(2) Acute circumscribed oedema, or Quincke's disease,—cases in which the oedema is fugitive, often affects mucous membranes, and in which there are no local signs of nerve disease.

(3) Milroy's disease, or chronic trophoedema, including cases of persistent oedema of segmentary distribution, and affecting one or more extremities, without local signs of nerve disease. Its hereditary or familial character is a marked feature of this form.

1. *Angioneurotic oedema* (hysterical paroxysmal oedema, Edgeworth) is an interesting transitional form between a vasomotor neurosis and a pure neuropathic oedema. The oedema generally involves an extremity, the upper limb quite as frequently as the lower. The onset is often sudden, and may definitely follow a nervous shock, or may be associated with the menstrual period. The swelling may involve a hand or an arm, or a leg or foot; its edge is often quite sharp, but may be ill-defined, corresponding only roughly to the boundary of the limb-segment.

In type (a), the blue oedema of Charcot, pain is common, and this is a true cutaneous hyperaesthesia, quite unlike the pain of Raynaud's

disease. The affected part becomes intensely hyperæmic, its colour varying from red to purple. Cyanosis and oedema occur in varying proportions, and when the oedema is great and the cyanosis slight, over the back of the hand, for example, it may well be mistaken for the result of suppuration in the palm. In my experience this error has occurred more than once, and once at least led to a fruitless operation.

Type (b) does not differ essentially from (a). The swelling in its character and distribution is the same, but the vasomotor phenomena are absent; and instead of hyperæsthesia there is commonly some degree of anaesthesia, or more particularly analgesia. There is no doubt that in both types the symptoms have frequently been unjustly ascribed to constriction applied by the hysterical patient. It will be noted that the "differentia" of the class is found in the presence of definite neurotic symptoms.

2. *Acute circumscribed oedema (Quincke's disease)* has affinities rather with the urticaria group of dermatoses than with the angioneuroses, though transitional forms to the latter may be found. Since Quincke's description was published in 1882 a large number of cases have been reported. The symptom-group has a strong tendency to occur in families—for example, in the series recorded by Dr. Ensor, in which 49 cases were met with in a family of 141 members, spread over seven generations. But even where the precise form of the disease is not reproduced, there is in the large majority strong evidence of a neuropathic inheritance. The symptoms may appear at any age, and in an intermittent form may persist till death. They consist in the rapid or sudden development of swellings, which may affect either the skin and subcutaneous tissues or the mucous membranes. They may affect either the trunk or limbs, and in rare cases probably the brain (cf. Osler (37)). The swellings are firm, do not readily pit on pressure, and do not, as a rule, present any circulatory change, though this rule is by no means absolute. When the swelling affects mucous membranes, the consequences may be serious; oedema of the larynx has been repeatedly the cause of sudden death, and this termination may occur in several members of a family. Fritz records a family in which eight were affected in three generations, and of these five died suddenly from respiratory obstruction; 12 of Dr. Ensor's 49 cases died from suffocation due to oedema of the glottis. When it is the intestinal mucosa that is affected, the intense pain caused thereby may be not only serious in itself, but may lead to an erroneous diagnosis. The following case, which recently came under my observation, is an epitome of the disease:—

The patient is a man in the prime of life, and of fine physique, being an adept at all outdoor sports. In early life he suffered from asthma, and is evidently of the neurotic temperament. For several years past he has been liable to attacks of abdominal pain, which are often associated with sudden swellings in various parts of the body. Sometimes it is a leg, which swells up to such an extent that he can hardly get his trousers on, sometimes an arm. The attacks are becoming more frequent and more severe, and now occur every



ten or fourteen days. He was told by a distinguished physician recently that he suffers from biliary colic, and that an operation was necessary. There are no physical signs of disease, except when the swelling is present. This shews itself as a general turgidity of the limb, so that the skin is stretched and shiny. Pitting is obtained, but not so much as one would expect from the degree of the swelling. The circulatory condition is very little altered to appearance. There are no urticarial wheals, but dermatographia is noted. The arterial pressure is 110 mm. of mercury. The coagulation-time of the blood is rather short—fifty seconds; but there is no other change. In spite of this it was thought well to try a course of calcium lactate, and this was done, but without effect. A short time after this examination the patient had sudden oedema of larynx, and his life was saved by tracheotomy. A few months later, after exposure to a cold December wind in a long motor ride, there was recurrence of urgent dyspnoea, and again tracheotomy was just in time to save his life. When last heard of the patient was being treated by hypnotism, but so far without any definite effect.

3. *Milroy's disease*, or *chronic trophoedema* to adopt the nomenclature suggested by Meige, is an oedema which develops without any apparent cause, and most commonly affects the lower extremities. Isolated cases are on record (Courtellemont), but typically it is familial or hereditary in distribution. The pedigrees of eleven families in which this condition occurred have been drawn out by Dr. W. Bulloch. The disease may be congenital or acquired. The individual affected may not shew any signs of nervous disease, though, with few exceptions, the descent betrays the stigmata of neuropathic inheritance. Not infrequently Milroy's disease occurs in association with, or in exchange for, other trophoneuroses; for example, with urticaria, with intermittent hydrarthrosis (Monro and Gregor), with Quincke's disease (Cassirer), with erythromelalgia (Courtellemont). In itself it has little tendency to shorten life. Courtellemont's patient was born with it, and was fairly active at the age of eighty-three; whilst members of the remarkable Wherrell family, recorded by Drs. Hope and French, had had the affection for more than sixty years. The oedematous limb is generally pale, but it may be cyanotic or hyperaemic. There is pitting on pressure, but the consistency is firmer than that of ordinary oedema. Even after many years' duration there may be complete absence of hypertrophy; but this is exceptional, and more commonly a state of mild elephantiasis is reached. It is not clear upon what this difference depends. Many members of the Wherrell family are described as suffering from "acute attacks"; in these the affected limb became still more tense and swollen, and the redness of the skin suggested an erysipelatous inflammation. At the same time there were constitutional symptoms of some severity, consisting of rigors, fever, abdominal pain, and in some instances vomiting. Dr. French draws a striking comparison between these attacks and the paroxysmal seizures of Quincke's and Raynaud's disease. The suggestion is tempting; but it must be remembered that somewhat similar seizures occur both in filarial elephantiasis and in the artificial form which occasionally follows the surgical



removal of inguinal glands (Riedel). Whatever may be the true explanation of these attacks, there is no doubt that they play a part in the production of the elephantiasis-like condition, though hyperplasia may occur without them.

The diagnosis of Milroy's disease from other forms of oedema depends upon the following characteristic features:—(a) The absence of all recognised causes of oedema outside the nervous system. (b) Its extreme chronicity, the affection dating sometimes from birth, and lasting for the remainder of life at whatever period it starts. (c) The sharply defined boundary of the swelling, and the tendency to affect segments of limbs rather than to follow the law of gravity, as in ordinary oedema; for example, the leg may be grossly diseased and the foot almost normal. (d) The tendency to produce a hyperplasia of the skin and subcutaneous tissues of the part affected. (e) The familial and hereditary character of the complaint, and its association, either in the affected individual or in other members of the family, with other neuroses.

*Intermittent hydrarthrosis* is fully described in Vol. III. p. 60.

*Secondary changes* in the tissues of neuropathic oedema do not occur as a rule. *Necrosis* is certainly rare; an example is recorded by Kreibich and Pollard in a remarkable case in which attacks of mental disturbance were attended by extreme tachycardia and the appearance of symmetrical plaques of exudation, which subsequently underwent necrosis. *Hyperplasia* has already been referred to as a sequel of acute inflammatory attacks, but it also occurs apart from such a history. In Courtellemont's patient there was some increase in the soft tissues, but the change was slight, and there was nothing resembling true overgrowth of the part; whilst in a similar case in which the oedema had been present for many years Dr. Rolleston specially notes the absence of any hypertrophy. On the other hand, in long-continued cases of Raynaud's disease, as well as in the pure form of trophoedema, distinct overgrowth of the part may follow. The hand, if it is in the upper extremity, gets a characteristic plumpness in which the normal creases disappear, the knuckles are marked by dimples, and the general aspect of the member is that of childhood. The contrast, however, is very great between the very moderate degree of hyperplasia found in such cases as these and the elephantiasis which results from lymphatic obstruction due to filariasis.

Before finally dismissing this section of the subject, a word of warning may not be out of place against the implicit acceptance of every case of obscure oedema as dependent upon the nervous system. Attention has been repeatedly called to the remarkable way in which the types recognised as neuropathic shade imperceptibly not only into one another but also into conditions with which the nervous system has nothing to do. If a case fail to satisfy the general rules of diagnosis just laid down, the mere fact that it does not conform to any other type does not justify its inclusion among the neuropathics. We may provisionally recognise an *essential oedema* which may be supposed to depend upon a

change either hereditary, congenital, or acquired in the permeability function of the capillary. A good example of this is Courtellemont's case of a remarkably healthy old man who had an oedematous leg at birth, and still retained it at the age of eighty-three without shewing either in his own history or that of his family any indication of nervous instability. To claim such a case as an instance of a neuropathic oedema certainly has an aspect of temerity, and it is probably wiser to place it in what an accountant would call a suspense account under the non-committal name of essential oedema as suggested above. Cases, however, do occur which, so far as the physical condition of the patient is concerned, correspond closely with the one now under discussion, and which, on collateral evidence, we do not hesitate to rank amongst the neuroses; it is indeed by no means improbable that as our knowledge of these conditions widens we shall feel justified in admitting their representatives more freely to the neuropathic fold. But, on the other hand, the reverse may occur. There are strong reasons for believing that not only in Raynaud's disease but also in cases of the Quinke type the tendency to oedema may involve the nervous centres themselves, giving rise to transient hemiplegia or other paralyses (38, 51). If gross symptoms may be produced in this way, the same explanation may also account for the less striking nervous manifestations which constitute the neuropathic diathesis, and if this be so, it involves the collapse of much of the evidence upon which the conception of a neuropathic origin for this particular group of oedemas is based. A full discussion of this subject, however, is beyond the scope of this article, and the possibility is mentioned here only to illustrate further the necessity for caution and an open mind.

III. TROPHIC LESIONS WITHOUT EVIDENCE OF AFFECTION OF EITHER THE VASOMOTOR OR VASO-PERMEABILITY FUNCTIONS.—The lesions hitherto considered have been estimated in terms of vascular derangement. Those that remain, the affections of bones and joints being reserved for consideration later (p. 95), may be grouped as (*a*) Hyperplasias, (*b*) Hypoplasias, and frequent combinations of the two.

(A.) **Hyperplasia.**—As might be expected this, apart from obvious vasomotor action, is rare. Examples of overgrowth following injury or disease of peripheral nerves are on record, but they are so few that no conclusions can be based upon them (59, 60). Syringomyelia provides the most numerous and clearest examples of neurotic hyperplasia. Two forms are met with; one is a pure overgrowth of the limb, which on more than one occasion has been put on record as a combination of syringomyelia and acromegaly (23). The resemblance is, however, merely superficial; unlike acromegaly one limb only is affected, and all confirmatory signs of that disease are wanting. It is now fully recognised that the hypertrophy which was attributed to acromegaly is but another manifestation of deranged nervous influence. This overgrowth may affect bones and soft tissues in equal proportion, or the change may mainly implicate, and this

is usual, the soft parts. The second type of hyperplasia is the *main succulente* first described by Marie, which consists of enlargement of the extremity due to changes in the soft parts only. There is no true oedema, but the skin and subcutaneous tissues are remarkably soft and redundant; the state is in fact identical with that already mentioned as an occasional sequel of a trophoedema or of Raynaud's disease. These hyperplastic conditions are closely but not invariably associated with neurotrophic affections of the joints or of the skin of the limb involved.

*Sclerodermia* can be but briefly referred to here, as it is fully described in Vol. IX. In a certain proportion only of the cases can the seat of origin be placed in the nervous system, but these are so numerous and so clearly authenticated that they constitute one of the most important instances of trophoneurotic action (von Notthaft). They are particularly important to the present argument, as they shew most clearly every gradation from the vasomotor neurosis, through affection of the vaso-permeability function, to a pure hyperplasia or hypoplasia of the cutaneous and subcutaneous tissues. The condition is so frequently associated with Raynaud's symptom-group that it has been regarded as a mere variety of that disease. At times the vasomotor phenomena precede the indications of sclerodermia by long periods; or, as in a case of Prof. Osler's (39), there may be sclerodermia of one part of the body and vasomotor phenomena in another. Passing from these vasomotor antecedents to the disease itself, it is recognised in three stages which, however, need not all appear in each individual case; they are the oedematous, the indurative, and the atrophic. Any of these phases may occur under neurogenic associations; for example, with atrophy of one-half of the body (Steven), with facial hemiatrophy (Dana), with a distribution corresponding to peripheral nerve areas (Hutchinson, Cassirer (fifth nerve)), or to nerve-root areas (Brissaud), or to Head's segmental areas (Drouin). They may occur also as incidents in organic nerve disease, as in syringomyelia (Schlesinger) or tabes (von Notthaft). Clearly sclerodermia is entitled to be classed under any or all of the headings of this article; it is placed here because its most representative phase appears to be that of hyperplasia.

*Sclerodactyly* is rather a subdivision of sclerodermia than an independent disease; it is particularly noteworthy on account of the atrophy of the bones as well as of the soft parts.

(B.) **Hypoplasia.**—That atrophic conditions of the skin and other soft tissues may be due to derangement of nervous influence is already apparent from the examples just mentioned, and any further illustrations which might be quoted are much complicated by the results of disuse or of loss of sensation or of both. Dr. Head has shewn how a retardation of growth may be produced from disuse alone, and how massage is able to maintain growth at the normal rate even when nervous connexions are altogether severed. He draws a sharp distinction between the skin which has been deprived of its nerve-supply and the "glossy skin" with pain and hyperaesthesia due to nerve irritation. The latter has already been described (p. 82), the former has the following characters

(22): It is dry, inelastic, and wrinkled; where not exposed to friction the epithelium is apt to accumulate in scaly masses, but when these are cleared off the underlying surface is pinkish-blue in colour and cold to the touch. In consequence of the associated anaesthesia, injury is particularly likely to occur and may lead to extensive ulceration, but it is very doubtful if any further change takes place spontaneously. Apart from the destructive changes which are due to infection the condition is a true hypoplasia of the superficial tissues, although the heaping up of the epithelium superficially suggests hypertrophy.

Facial hemiatrophy has been referred to already in its association with scleroderma and syringomyelia. A full description will be found on p. 167.

IV. TROPHONEUROSES OF COMPLEX CAUSATION.—It is curious that those lesions which are most closely connected in our minds with trophoneurotic action are those the interpretation of which is most open to criticism. They are destructive processes complicated by infection, and originate under conditions most unfavourable to tissue nutrition, either by reason of anaesthesia or constant fouling by excreta, or both. They may conveniently be considered in two groups—acute and chronic.

*Acute Decubitus or Bed-sore.*—Open lesions in the form of acute decubitus are met with most frequently in acute myelitis, and more particularly in infective meningo-myelitis. It cannot be said that this lesion shews any absolutely characteristic feature, the extreme rapidity with which it may appear constituting its chief claim to a place among the trophoneuroses. Within twenty-four hours after the commencement of the illness the buttocks may turn a purple colour and undergo the most extensive necrosis. Even allowing for the fact that the conditions are in the highest degree unfavourable for the preservation of nutrition—the patient paraplegic, with complete loss of control over the sphincters, and anaesthetic, even if not actually unconscious—it is difficult to resist the conclusion that changes in the nerve-supply are playing a direct part in the process. Sir W. Gowers points out in this relation that the primary disease is often irritative as well as paralyzing, and suggests that this quality is responsible for the trophic disturbance.

Closely analogous to this are the ulcers seen in connexion with “glossy skin”; in this condition vesicles may appear spontaneously, where there is no question of pressure, and form the starting-point of an ulcer. This commonly remains superficial, and does not extend as is likely to be the case where there is anaesthesia, but as to its neurotrophic origin there seems to be no doubt. Neuropathic keratitis, the pathology of which is still a subject for dispute, offers a very close analogy to the acute bed-sore.

*Chronic Lesions.*—The chronic members of this group stand on a very different footing; in these a neuropathic element is certainly present, but it is only one of the difficulties with which the nutrition of the part has to contend, and its importance can be judged only by weighing the



circumstances in each individual case. The acute bed-sore has just been mentioned as an example of a true trophoneurosis, on the ground that the same result cannot be brought about in the same space of time by other means. On this standard the chronic bed-sore can hardly be admitted to the list at all; it does not differ in mode of development or final appearance, whether it occurs in a case of paraplegia or one of enteric fever; at the most the difference is one of degree only, and each case must be judged on its merits.

Perforating ulcer is the most characteristic member of the class, but even it is not peculiar to diseases of the nervous system. An acute form has been described, but the recognised type is chronic. The most common seat is under the ball of the big toe. It is preceded by a corn; not an unusual phenomenon in that region, but in these cases very often on an exceptional scale which may itself be a result of changes in the nerve-supply. The early stages may be altogether unobserved, as they consist of inflammatory or necrotic processes in the bursa beneath the corn, and by the time the pus makes its way through or by the side, the destruction of tissue has probably reached down to the bone and perhaps opened into a joint. In this way the perforating ulcer may have reached its full development at what appears to be its start. Its essential quality is painlessness, and it may be met with as a result of any lesion which interrupts the afferent path without interfering with locomotion. It is thus met with most commonly in tabes, but is found also in spina bifida and injuries to the sacral plexus. If the patient be put to bed at any stage of the disease the ulcer heals in precisely the same way as any other ulcer of corresponding depth.

The painless whitlows of syringomyelia and the mutilations of leprosy are the perforating ulcers of the upper extremities, and in them too is found that fatal lack of the warning sense of pain without the paralysis which would make that warning unnecessary. Dr. Head has shewn that the identical lesions which occur in certain cases of injury to the brachial nerves synchronise in their appearance and disappearance with the loss and regain of protopathic sensation (20). This is the limit of our certain knowledge of their causation. Mere absence of sensory impulses cannot cause death of tissue, and how far this absence may make a part more sensitive to the effects of injury, or how far it may interfere with its recovery, is by no means clear. That it has some influence of this sort is strongly suggested by an incident which recently came under my notice. In a case of tabes a single application of linimentum iodi produced sloughing of the skin over the ankle, to which it had been applied for the relief of referred pain. The skin previously had a healthy appearance, and the general nutrition of the patient was good. This seems a clear example of lowering of nutrition from nervous causes without any apparent vasomotor change, but even this falls far short of a primary necrosis from nervous causes.

**Conclusions.**—(1) That the influence of the nervous system over nutrition is complementary to local and presumably non-nervous mechan-

isms, and that its derangement will become apparent only when the resources of the local machinery are exhausted.

(2) That evidence points to the neuro-vascular mechanism as the intermediary between the nervous system and nutrition.

(3) That both the afferent and efferent paths are, in some if not in all cases, by vasomotor nerves, and may travel in the same nerve.

(4) That this mechanism is of two kinds; one which regulates the calibre of the vessels, the other which effects changes in their permeability. That the two portions of this mechanism are commonly associated in their action but may act separately. Derangement of either the vasomotor or vaso-permeability mechanism may occur at any level of the nervous system, and may be due to either functional or organic change.

(5) With regard to the causation of nutritive lesions which are not obviously connected with vascular changes, there is collateral evidence in their clinical and pathological associations that it is still the neuro-vascular mechanism which is at fault; at all events there is no evidence of the existence of independent trophic paths.

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## NEUROTROPHIC AFFECTIONS OF BONES AND JOINTS

**Introductory.**—The conception of trophic centres which control the nutrition of the bones and joints was formulated by J. K. Mitchell, as far back as 1831, in an article on the occurrence of arthropathies as sequels of disease or injury of the spine. Mitchell even suggested that the articular lesions in rheumatic fever might be due to changes in the nervous system. Although these hypotheses did not meet with general acceptance at the time, their influence is shewn by occasional records during the next thirty years of arthropathies following various affections of the brain and spinal cord. But it was not till 1868 that Charcot described the trophic lesions of tabes dorsalis, the first case in this country being reported by Sir Clifford Allbutt in the following year. Charcot's observations established once for all the existence of the joint disease which bears his name, and on which such a large part of our knowledge of nervous arthropathies depends. His work, indeed, was so complete that little remained for subsequent observers except to offer explanations, and to fill in details. The power of his name at once secured him a respectful hearing, and, in France at all events, a ready acquiescence; but elsewhere, particularly in Germany, his views met with most strenuous opposition, which indeed is not even yet silenced. Virchow, Volkmann, and Strümpell contested his deductions; and so great was their influence that, for ten or fifteen years after, while records of Charcot's disease were numerous in France and fairly common in England, in Germany their scarcity was remarkable.

Weir Mitchell's description of spontaneous fractures in tabes, in 1873, formed an addition to our knowledge of hardly less importance than Charcot's of 1868. This was followed at a very short interval by further observations from Charcot, who early saw the intimate relation between the changes in the bones underlying spontaneous fracture and those which



form the basis of affections of joints. It was some years, however, before this connexion received wide recognition, and during this period the osteopathies failed to attract the universal interest which had been so rapidly given to the arthropathies. But since then the history of the two affections has become inseparable, and justly so. During the 'eighties the numerous records in every literature prove the increasing interest in both aspects of the disease; this was intensified in the latter half of the decade by the recognition of similar changes in syringomyelia. Since then, our knowledge of the neurotrophic affections of the skeleton has been widened in various directions, but Charcot's disease still retains a position as unique as when it was first described. Its close connexion with two such remarkable diseases as tabes and syringomyelia, its frequency, and lastly its pronounced characteristics, combine to produce a clear-cut clinical picture which in this field is without a rival.

In the following pages it will become apparent that the direct effect of the nervous diseases upon the bones and joints is a simple one, namely, an atrophy anatomically indistinguishable from that produced by inactivity and other causes. But, whereas in all other neurotrophic lesions immobilisation is ensured either by pain or paralysis, so that the condition remains in its primal simplicity a pathological rather than a clinical phenomenon; in Charcot's disease the osseous change is activated, so to speak, by the continued use of the damaged limb, so that what is ultimately recognised at the bedside as a Charcot's joint is not a pure trophic lesion, but a medley of secondary pathological changes. It has, however, attained to a clinical importance which all other trophic affections lack, and the main part of this article will therefore be devoted to a description of the osteopathies and arthropathies occurring under these conditions. They will be taken as types of such affections and will be used as a standard of comparison in dealing with others.

## PART I.—TROPHIC LESIONS IN TABES AND SYRINGOMYELIA

**A. Osteopathies.**—*Spontaneous Fracture.*—The occurrence of spontaneous fracture gives the first and, as a rule, the only clinical evidence of trophic change in the bone, though after the event it has often been realised that lightning pains have been especially severe in that limb, and in more than one instance pain had been referred to the spot for months or years before (Pitres and Vaillard).

Fractures occur most frequently in the long bones, but may affect any part of the skeleton. Where the short bones, such as the vertebrae and tarsus, are affected the condition becomes so complex and characteristic, in consequence of changes set up in the adjacent articulations, as to require a special description under the heading of the osteo-arthropathies. But even in the long bones there is a marked tendency for fracture to occur in a limb which is already the seat of an arthropathy, and in that part of it which is in immediate relation with the diseased joint. The fractures,



as will be seen later, shew in their distribution a general correspondence with the level of the primary disease in the nervous system.

All that is implied by the term spontaneous is that the obvious cause is inadequate to produce the result. The degree of inadequacy is very variable; it may be extreme, as in cases in which the mere act of turning over in bed has sufficed to break the femur. In one case fracture of the humerus occurred while the patient was pulling on his boot, and a patient under my care fractured his femur in the act of stooping. It has been argued that the clumsy, inco-ordinate movements of a tabetic account for an apparently spontaneous fracture; but as a considerable proportion of these fractures occur in the pre-ataxic period, and, moreover, as they are even commoner in syringomyelia than in tabes, this view cannot be accepted. My patient broke his thigh twenty-five years ago, and even now the ataxia is of the slightest. After their spontaneity the most conspicuous feature of these fractures is their complete painlessness. This is so absolute that, unless the injury be such as to render locomotion a physical impossibility, the patient will continue to get about on the broken limb without any suspicion of what has occurred. Apart from this insensibility, the fracture does not present any characteristic features, though it is stated that the line of fracture tends to be transverse instead of being as usual oblique, and that the amount of bony displacement and of swelling of soft parts is usually excessive. The process of repair sets in with at least the usual rapidity; but exceptions to this rule have been described, in which little or no attempt at union took place (Rivington). The amount of callus is nearly always abnormally great; and, even if allowance be made for the rough treatment incidental on the painlessness of the parts, it is probably still in excess of what is formed under other conditions. Occasionally a union which has been effected under the shelter of an enormous mass of callus again gives way without any apparent cause except the absorption of the new material.

The incidence of spontaneous fracture in tabes is in the large majority of instances upon the bones of the lower extremities. Its tendency to occur in the immediate vicinity of a joint which is already the seat of similar change makes it impossible in many cases to consider it apart from the arthropathy. Among the short bones, those of the foot are often affected, and less commonly the vertebrae fall victims, but both of these will be considered more in detail on page 105. A remarkable trophoneurosis is that of the alveolar process of either maxilla. Of this, if we include the painless loss of sound teeth, no less than twenty-three instances are on record (Rosin, Kalischer). In some of these a fracture occurred which was in the literal sense spontaneous, in others the whole of the alveolar process came away with the extraction of a tooth (Sabrazès and Fauquet). In some cases simple atrophy occurred, in others actual necrosis with ulceration.

The fractures may be multiple; in a recent series of sixty-one tabetic patients there were seven instances of multiple fractures; of these seven, five had two fractures, one had four, and one no less than seven. In a

case of Charcot's (a life-sized model of which he presented to the St. Thomas's Hospital Museum) the fractures were even more numerous. These extreme cases, however, may possibly belong to a different category; for they generally occur in patients long bedridden and in the last stage of the disease, in whom, therefore, bony atrophy due to inactivity may be fully as responsible for the fractures as degeneration of the nervous system.

In syringomyelia a fracture shews the same spontaneity and the same painlessness as in tabes, but in the majority of cases it affects the bones of the upper limb instead of those of the lower. It is commonly accompanied by the various trophic affections of the soft parts of syringomyelia, such as vasomotor disturbance with or without a trophic oedema or muscular wasting and paralysis, whilst very often trophic whitlows or even gangrene point to an infective complication. The fracture has the same close relation to an arthropathy as in tabes.

**B. Arthropathies.**—Arthropathies may occur at any stage of tabes, and not infrequently are the first serious indication of the malady. Even in the affected limb analgesia of the joint may be the only sign of nervous change; and this may be present without implicating cutaneous sensation. As a rule, however, a careful examination reveals more definite signs of the spinal disease. In about 75 per cent of the cases in tabes the joints affected belong to the lower extremities. Thus, out of 268 tabetic arthropathies collected by Chipault, 207 were in the lower limbs; of these, 120 affected the knee, and 57 the hip. It has been noticed that, when the lesion affects the articulations of the upper limbs, it is in the late stage, when the tabetic change has spread to the cervical region of the cord. With the exception of those of the feet, which constitute a special group (*vide* p. 102), the smaller articulations are but rarely affected. In the list of 268 arthropathies just quoted the wrist-joint figures three times, the finger-joints twice, and the temporo-maxillary articulation once. Frequently the arthropathies are multiple, and then most commonly symmetrical. A joint which has been damaged in any way is specially prone to be attacked; as in an old fracture of the wrist recorded by Chipault, or in the dislocation of the hip mentioned by Virchow. As in tuberculous arthritis, slight injuries may precipitate an attack; though the possibility of intracapsular fracture must then be considered.

*Premonitory symptoms* are completely absent in the large majority of cases; but the history commonly shews that the onset of the arthropathy has been preceded by pain referred to the articulation, which may either resemble lightning pains, or be rheumatic in type and vary with changes in the weather. In one instance this prodromal symptom had lasted for twenty-three years (Tournier), in another for thirty.

*Onset.*—As already pointed out, an arthropathy may immediately follow an injury which is so trivial that under ordinary conditions it would be quite inadequate to produce any serious result. Very frequently even this slight traumatic factor is absent, and the joint affection appears

as a bolt from the blue. The patient wakes up in the morning and finds that one knee is much swollen; or, as he is walking in the street, his leg suddenly gives way under him (Marie).

At least as remarkable as the suddenness of onset is the complete painlessness of the condition. In consequence of this absence of pain the amount of disability produced by the grossest disease of joints may be almost incredibly small; for example, a patient with arthropathy of the knee continued to shoot on foot for a whole season until dislocation occurred (Strümpell). Painlessness then may be regarded as the pathognomonic sign of this form of nervous arthropathy; exceptions to this rule have been recorded (Fort), but they are few; and even in them the pain was transient, and present only at the outset. In these cases it may probably be regarded as analogous to anaesthesia dolorosa.

*Clinical Condition.*—In the first stage the joint is distended with fluid to a degree rare in any other disease. In many cases the effusion is not confined to the articulation, or even to the surrounding tissues, but infiltrates the whole limb. In either event the result is to produce a characteristic solid oedema which pits but slightly on pressure, and the extent of which varies within the widest limits. The extreme distension renders the skin over the affected area white and shining, and the subcutaneous veins become unduly visible. Palpation may not reveal anything in the joint, but if the swelling be less extreme than has been described, it is often possible to elicit crepitus, or to detect the presence of loose bodies and even of irregular fragments of bone within the articular cavity. Both active and passive movements may be freely carried on without causing the patient the least inconvenience; and already an abnormal degree of mobility may be apparent.

In this, the first, stage all joints present to a great extent a similar condition; but with the absorption of the intra-articular effusion and the subcutaneous oedema—a process which may take weeks or months—and the evolution of the second stage, a notable difference between the various articulations becomes obvious. The morbid process may be considered as made up of two opposing factors, both acting on the osseous elements of the joint; but one leads to rarefaction and absorption of the bone, the other to hyperplasia. It is noteworthy that the relative activity of these opposing forces varies with the nature of the articulation (*vide* also p. 106). In the ball-and-socket joints, such as the hip and shoulder, the atrophic factor predominates; whereas in the hinge-joints, such as the knee and elbow, overgrowth carries the day. A group of cases of considerable clinical importance forms an apparent exception to the statement that the arthropathy of the hip is of the atrophic type, and the course of these cases is so characteristic as to deserve a separate mention. They commence suddenly in a manner very strongly suggesting spontaneous fracture of the upper end of the femur, and come under observation with a huge mass of bone enveloping the outer aspect of the os innominatum, or, as in one instance, arising from the iliac fossa and filling the lower quadrant of the abdomen. Two such cases have recently



been under my care. One was a man of seventy-two, who in 1883, twenty-five years before, while stooping, suddenly felt his left thigh give way beneath him without pain. About nine months later he was admitted into hospital with a large tumour in the region of the left hip-joint, which was explored in the belief that it was a sarcoma of the upper end of the femur. The other patient, a man of sixty-one, gave a precisely similar history, except that the onset was thirty years ago instead of twenty-five. In both the mass of bone about the hip-joint is as large as two fists, and in both the ordinary signs of tabes have appeared only within the past few years. These cases are by no means infrequent (cf. Klippel and Monier-Vinard, Gibert), and the real danger that they may be confused with tumour renders them of practical importance. In the shoulder-joint the corresponding condition may be found, but is less common; I know of one such case in which amputation was performed, almost certainly under an erroneous diagnosis.

In the ordinary hip-joint type the atrophic process leads to a rapid destruction of the head, neck, and even of the trochanteric region of the femur; and displacement is the common result. There is some compensatory formation of osteophytes at the margin of the acetabulum and about the trochanters; but, as a rule, these are of no great size or extent, and they may be completely absent.

On the other hand, when the disease attacks the knee or elbow, the outgrowths of bone, particularly about the head of the tibia and patella, are commonly so extensive as to constitute the most prominent clinical feature. Atrophy, however, does occur; but, since it affects the femoral condyles and central part of the tibia, it is masked by the presence of outlying bony deposits. At a late period the articulation may become immovably fixed by osseous ankylosis; but more frequently it passes into the other extreme of abnormal mobility.

The joint lesions in tabes and syringomyelia are practically identical, such differences as do exist being found rather in the frequency with which they occur, and the parts of the skeleton which they affect, than in any anatomical peculiarity. In the first place, their relative frequency is considerably greater in syringomyelia than in tabes; in the latter disease the proportion of cases which present joint lesions is not more than 3 or 4 per cent; in the former the lowest estimate would place it at 10 per cent (Sokoloff), the highest at 40 per cent or even more (Schlesinger). Again, whereas in tabes the lower extremities, as compared with the upper, are affected in at least 75 per cent, in syringomyelia the proportion is reversed, the incidence being in about 80 per cent of the cases on the bones and articulations of the upper limbs. Out of 97 syringomyelic arthropathies, 29 involved the shoulder-joint, 24 the elbow, and 18 the wrist (Schlesinger). In tabes the trophic lesions shew a striking tendency both to multiplicity and symmetry; in syringomyelia, on the other hand, whilst there is an even greater tendency than in tabes to multiplicity, that to symmetry is lost. In syringomyelia, again, suppuration with necrosis is fairly common; and though this may be explained to a great extent by



the presence of trophic ulcers which, as in the tabetic foot, favour infection, this does not apply to all cases. In a patient under my care with typical *pièdes tabétiques* of syringomyelic origin, bony sequestra had been thrown off from both feet for more than six years, but a permanent perforating ulcer existed on one side only.

C. **Osteo-Arthropathies.**—The precise nature of the *vertebral lesions* has been the subject of much discussion, though their symptomatology and morbid anatomy have now been clearly established by Krönig, Abadie, and others. They are extremely rare in comparison with those of other bones and joints in tabes. For example, they do not appear in Chipault's collection of 268 tabetic arthropathies. A few years later, however, Abadie collected 13 cases, some from personal observation, some from literature. As with the pure arthropathies, the onset may be insidious or sudden. In the former event the patient notices a gradually increasing spinal curvature, which may be either kyphotic or skoliotic, but in nearly all tabetic cases at all events centres about the lumbar region, just as in syringomyelia it is the cervico-dorsal which is at fault. When it is sudden, the onset may be precipitated by some slight shock—a slip in walking in one case, in coming downstairs in another—or a sharp angular curve may appear quite spontaneously. In all cases alike pain is absent or insignificant, and interference with the power of locomotion is slight, and such as there is depends upon loss of mechanical support and not upon injury to the spinal cord or nerve-roots. The immediate cause in cases with a sudden onset is clearly spontaneous fracture. In a patient with the fracture in the lumbar region the fragments could be slid one over the other without pain, and the displacement was so considerable that the patient himself noticed the projection of the luxated portion into the abdomen as a palpable tumour. Even with such deformity, symptoms of pressure on the cord are rare.

The frequency of spinal curvature in syringomyelia has added to the difficulty of deciding as to its inclusion among the trophoneuroses. There is little doubt that, in some cases, the explanation of the deformity is weakness of the spinal muscles; Roth and others, indeed, argue that this applies to all cases, and this view has received some support (Londe and Perrey); but most authors favour a trophic origin (Schlesinger, Bruhl, Morvan), and the question may now be considered as finally answered in the affirmative by the pathological evidence adduced by Borchardt and Nalbandoff (*vide* pp. 103, 105). There is no record in syringomyelia of a complete solution of continuity in the vertebral column such as has been described in tabes, but everything short of that has been found; the curvature, indeed, may reach a most extreme degree, far exceeding that usually attained in tabes, the difference depending not upon any greater intensity of pathological change, but upon the involvement of the higher regions of the spinal column. Pathological evidence apart, it is difficult to account for the acute accession of the deformity sometimes seen on any hypothesis other than that of trophic change in the bone. The abnormal softness of the bones, upon which Borchardt lays stress,



seems to afford the most reasonable explanation of such a sequence of events.

*The Tabetic Foot.*—In 1881 the first case was described and the patient shewn by Mr. H. W. Page; and in 1883 Charcot recorded his first observation, coupled with an inexplicable claim for priority. As in the case of the vertebral changes, it may be ranked either among the arthropathies or the osteopathies; for consideration of this point see p. 108.

The tabetic foot occurs with unusual frequency in the early stage of tabes, and often in the pre-ataxic period (Trömner and Preiser). Its onset is commonly abrupt, and nearly always painless. If seen in the early stage, the only obvious change may consist in an abnormal swelling of the back of the foot (Marie); but, as a rule, the characteristic deformity is fully established before the patient comes under observation. The foot has then acquired a most distinctive quadrate or truncated appearance, which has been aptly likened to the artificial deformity of the Chinese lady; the arch has completely disappeared, and the toes look as if they arose immediately from the tarsus; the explanation of this is that the metatarsus may be dislocated either above or below the proximal part of the foot. The malleoli are generally much thickened, and, in consequence of the collapse of the calcaneum, often rest on the ground. The ankle-joint may shew a characteristic arthropathy, and thickening may extend some distance up the bones of the leg. The soft tissues of the foot are the seat of a hard oedema, and the skin is often distinctly hypertrophied. Manipulation elicits bony crepitus, which is often so distinct and diffuse that the foot may feel like a bag of bones. Frequently, though by no means always, these processes are accompanied or preceded by perforating ulcer, which, by means of secondary infection, may cause necrotic changes in the metatarsus or phalanges.

In a second variety of trophic foot the osseous changes appear to depend entirely on the presence of a perforating ulcer with its attendant infections. The necrotic process begins at the base of the ulcer, and steadily extends until, in the course of years, perhaps, a large portion of the skeleton has been exfoliated; the resulting condition closely resembles that of the pure tabetic foot. This should, however, still be regarded as a complicated trophoneurosis of the subcutaneous or cutaneous rather than of the osseous tissues (p. 93).

**Morbid Anatomy.**—A. *Changes in the Bones.*—It is not uncommon for spontaneous fracture, especially in tabes, to remain unexplained by morbid anatomy. Series of cases of spontaneous fracture have been recorded by competent observers (Schnltze, Baum, Kienböck), in which the most careful examination failed to shew the expected osseous changes. It is suggested that there may be modifications in the internal architecture, which render the bone unable to resist the strains to which it is exposed by lack of sensory warnings on the one hand, and deficient co-ordination on the other; but the existence of such change is at present a pure assumption. The special liability to fracture, which is observed in the neighbourhood of an arthropathy, may be due to the

atrophic change to which, as Sudeck (77) has shewn, the bones for some distance from a diseased joint are prone, but direct evidence of this is often lacking.

In syringomyelia, to a much greater extent than in tabes, changes in the bones of the most varied nature have been found (Nalbandoff, Tedesko, and others). The most characteristic is a rarefying osteitis which may affect the whole of one of the long bones, or may extend to a whole limb. Both spongy and compact tissues are of a looser and more open texture than normal, and this may be visible not only to the x-rays but to the naked eye. In addition to, or instead of, this atrophic process there may be fresh deposits of bone most commonly as osteophytes, but sometimes as a plug of dense bone filling up what should be the medullary cavity, or causing an increase in the density and amount of the compact tissue (Raymond and Lejonne). Osteomalacia, due to absorption of lime salts, is also met with (Tedesko); but as this may also result from any infective inflammation, caution is necessary in accepting cases of this description as examples of neurotrophic disease. Chemical analysis of such atrophic bone shews a striking deviation from the normal, namely, a reduction of the inorganic elements from 66 to 24 per cent, and a relative increase of the organic constituents from 33 to 76 per cent. The loss of inorganic matter falls mainly on the phosphates, the proportion of which sinks from 50 to 10 per cent; whereas the ratio of fat rises to 37 per cent (Regnard).

These extensive alterations in the bony tissues, occurring apart from disease of joints, which are more frequent in syringomyelia than in tabes, are almost constantly associated with trophic affections of the soft parts, which sometimes occur as a vasomotor disturbance, sometimes as trophoedema with or without overgrowth of tissue. In the light of the views already expressed (p. 85) it is clear that this association is not a mere coincidence, and to this point further reference will be made.

B. *Changes in the Joints.*—Even in the absence of an obvious arthropathy the joints of sufferers from either tabes or syringomyelia may be the seat of morbid change (Dupré and Devaux). Jürgens examined apparently healthy joints; and in those of larger size found relaxation of the capsule with elongation of the ligaments, which was often considerable. He further noticed hyperaemia of the synovial membrane and other soft structures, which he attributed to vasomotor disturbance of central origin. This laxity of the capsule to some extent explains the remarkable capacity for rapid and extreme distension which is displayed from the outset by the tabetic joint; it may also favour the operation of the traumatic influences which so often provide the exciting cause of the outbreak; but whether its importance is to be rated at a higher level than this is a matter for doubt.

Pathological observations during the earliest stage of an arthropathy, that is, during the period of effusion, are rare. The fluid, which may be sanguineous, is usually clear and of the nature of synovia. The joint capsule has been found distended, softened, and at times almost destroyed.



Hyperaemia of the synovial membrane with villous hypertrophy is common, as is also softening or even destruction of the articular cartilage; loose bodies are almost constantly present, and may either have been detached from the synovial fringes or result from an intra-articular fracture.

In discussing the fully established disease from the anatomical point of view, the clinical division into a hypertrophic and an atrophic form may conveniently be retained. It will be remembered that the former represents the affection of the knee and elbow, the latter that of the hip and shoulder; and, moreover, that the form has no relation either to the severity or the duration of the disease.

(a) *Hypertrophic Form.*—Outside the capsule bony deposits are specially apt to form; these may occur simply as marginal osteophytes about the articulation; or they may extend into the periarticular tendons and muscles, and be so considerable as to suggest an ossifying myositis (von Kahliden, Thomson). The capsule itself may be partially or completely ossified; or, on the other hand, may disappear by coalescence with the neighbouring soft structures. Within the joint the ends of the bones are greatly and irregularly enlarged by marginal osteophytes; the articular cartilage has in large part disappeared and the bone so exposed has a porous, spongy look; in very exceptional instances there is a subarticular layer of sclerosed, eburnated tissue as in osteo-arthritis. The changes in the bone extend far beyond the immediate neighbourhood of the articular surface. The rarefaction shewn by the orifices of the enlarged Haversian canals, by the loose texture on section and by its lightness, is present to the extreme limits of the capsule and even beyond. This change is present at a very early stage; it is responsible for the intracapsular fracture which is a common event in the evolution of an arthropathy, and must be regarded as the least common denominator of all forms of arthropathy. Not infrequently, however, a more or less complete bony union results between the opposed surfaces, and the final condition is one of ankylosis in place of the more usual flail joint. In most cases the synovial membrane is the seat of profuse villous overgrowth; and as a result the cavity may contain hundreds of melon-seed bodies which have become detached. But, though the prevailing note is hypertrophy, the activity of the opposite process can still be recognised in the wearing away of parts of the articulation.

(b) *Atrophic Form.*—In the neighbourhood of the hip- and shoulder-joints the tendency to the formation of bony deposits is comparatively slight, though indications of it may appear. Within the articulation it is altogether absent. The synovial membrane and other soft structures have completely disappeared; the dislocated femur or humerus has lost all its normal characteristics in the process of atrophy, and strongly resembles the drumstick to which Charcot compared it. Similar changes are found in the acetabulum, which is flattened out and has the same porous appearance which is noticed about the femur. In many instances the rarefactive process has extended far beyond its margins, and has involved a considerable portion of the iliac bone.



C. *Vertebral Lesions*.—It is difficult to say whether these should be ranked as osteopathies or arthropathies; without entering upon a barren discussion we may adopt the term osteo-arthropathy, which has the advantage that it does not imply any hypothesis. A considerable amount of pathological evidence has now accumulated (Abadie), but it cannot be said to add any new facts to those described first by Charcot and later by Pitres and Vaillard. In the patient observed by the latter the vertebral column became slowly deformed without any local pain; later there were formed around the spinous and transverse processes of the affected vertebrae "veritable osseous tumours accessible to palpation." At the necropsy the first lumbar vertebra was almost totally destroyed; the second shewed a remarkable osteophytic formation which covered its body and transverse processes, and led to a very considerable enlargement. The bodies of all the lumbar vertebrae and of the last five dorsal were covered with osteophytic deposits. The condition described corresponds very closely to that found clinically by Krönig. Borchardt, who has written exhaustively on the vertebral lesions of syringomyelia, describes a condition which in its broad outlines is precisely similar. The picture is one of central destruction with peripheral hyperplasia about the various processes of the vertebrae; the latter may be so extensive as to bury the heads of the ribs in masses of new bone. The bone, both old and new, is very soft, yielding readily to the knife, and to this quality Borchardt attaches a large share in the production of the deformity. To these new-formed bony buttresses, soft as they are, must probably be ascribed the remarkable immunity from pressure symptoms which these patients manifest.

D. *The Tabetic Foot*.—It is impossible to give any systematic account of the pathological processes which result in this deformity; for, in spite of the comparative uniformity of the clinical product, they vary infinitely. Where perforating ulcer coexists it may be necessary to distinguish the changes which take place in the anterior part of the foot from those which affect the posterior. In such cases it is only in the posterior part that trophic lesions can be studied in their purity; whilst in the region of the metatarsus and phalanges such changes, if existent, are hopelessly complicated by the presence of others due to the infection from without. Disease of the ankle-joint, though present in a large proportion of the cases, is not an integral part of the tabetic foot. It tends to assume the hypertrophic rather than the atrophic form, both the tibia and fibula (including the malleoli) being thickly overlaid with periosteal deposits. At the same time, the cavity of the articulation commonly extends, at the expense of its smaller neighbours, until most of the tarsal joints may be included within it (Targett). In the foot, however, atrophic processes predominate: all the bones are light, porous, and prone to fracture; the smaller ones either disappear entirely or remain as unrecognisable fragments, whilst the larger, and of these the calcaneum is the most frequently affected, collapse under the weight they have to support. The articular surfaces are eroded or, less frequently, connected by new bone. Displace-

ments are almost invariable, the most prevalent form being a dislocation of the anterior part of the foot, including the metatarsus either above or below the tarsus. To this the curious squat shape of the foot is largely due. In the metatarsal region, particularly when the trophic ulcer governs the situation, the bony structures are often completely lost, having undergone necrosis and been thrown off, or otherwise removed, through the wound. By the same process the metatarso-phalangeal joint is disintegrated, and one or more of the phalanges may have disappeared. At the farther limits of the area exposed to infection signs of osteoplastic periostitis are often evident; though elsewhere they may be conspicuous by their absence.

**PATHOGENY.**—Before discussing the subject from the neurological aspect we must disentangle certain features of the neuropathic joint which depend not on derangement of nervous influences but on mechanical factors, and are common to all forms of joint disease. As already pointed out, all the nervous arthropathies present a mixture of atrophy and hypertrophy, but in very different proportions. In certain joints, such as the shoulder and hip, atrophy predominates, whereas in the elbow and knee hyperplasia holds the field. In the joints of tabes and syringomyelia either or both of these processes may reach an extreme which is not found in other circumstances, but the general type remains the same for each articulation whether the disease is nervous, rheumatoid, or tuberculous; it is, in fact, determined by the anatomical character of the articulation and not by the state of its nerve-supply. Generally speaking, the ball-and-socket joints assume the atrophic form, the hinge-joints the hypertrophic. Further, atrophy tends to occur at the centre of the articulation, hypertrophy at the periphery. The explanation is probably to be found in the distribution of pressure within the joint; where this is uniform and continuous, atrophy takes place; where it is intermittent and variable in degree, the result is hyperplasia. In the hip-joint, for example, where the head of the femur is completely embraced by the acetabulum, and where, in consequence, pressure and friction are evenly distributed over every part, we find atrophy. In the knee the mutual adaptation of the articular surfaces is much less accurate, and varies in degree with the movements of the joint; it is most imperfect about the margin of the tibial head, which, even during active use of the articulation, may lie almost or altogether outside the zone of pressure. Consequently that part of the articular cartilage and bone becomes the seat of active hyperplastic processes, while the femoral condyles and the central part of the tibia may be undergoing an equally pronounced atrophy. The hyperplastic element in a nervous arthropathy may then be regarded as primarily of local origin; it finds its analogue in the various forms of chronic arthritis, and is the expression of a reaction to irritative processes initiated within the joint.

It might be thought that these indications of a local reaction to irritants and of a capacity for repair are incompatible with the loss of nervous control, but many reasons can be adduced against this supposition.

Union takes place with the formation of an exuberant callus in a bone which has undergone spontaneous fracture; to borrow an analogy from cutaneous lesions, the trophic corn exists side by side with the perforating ulcer, and the perforating ulcer itself heals readily in favourable circumstances. On the other hand, a belief in the local origin of the hyperplastic process need not entail a denial of a nervous factor which may modify the result. Though in their general outline the changes resemble those met with in non-nervous diseases, they differ very materially in their extent. In both tabes and syringomyelia the bone and joint lesions may shew a degree of bony overgrowth which is not met with in any other condition except tumours. It is impossible to decide whether the whole of this extreme hyperplasia can be accounted for by the continued use of the damaged joint, or whether it represents in addition what might be called an ataxia of reaction on a nervous basis.

Although, apart from these limitations, the direct dependence of these bone and joint lesions in a broad sense upon changes in the nervous system is now generally accepted, a short reference must be made to various divergent explanations which have been offered, mainly from German sources, in substitution of the trophic hypothesis. Two of these can be dismissed in a few words; they are Strümpell's hypothesis of a syphilitic, and Volkmann's of a traumatic arthritis. So long as the lesion was recognised in tabes only, with the almost invariable syphilitic antecedents of that disease, Strümpell's suggestion may have caused some hesitation; but with the recognition of precisely similar lesions in syringomyelia, with which syphilis has nothing to do, the hesitation disappeared. Volkmann's suggestion rested on the assumption that the affection of joints occurs especially in the later stages of tabes, when the ataxia is most extreme and injuries more likely to be received. It is now acknowledged that the joint lesions are not limited to any period of the disease, indeed they have rather a preference for the earlier stages and for those forms of it in which ataxia is slight. Moreover, their presence in syringomyelia, in which ataxia is commonly absent, dealt a final blow to the belief in their traumatic origin.

But Virchow's view that Charcot's disease is simply osteo-arthritis in a patient with tabes or syringomyelia deserves fuller consideration and is more difficult to set aside. Although the clinical differences are great, it must be confessed that the morbid anatomy is remarkably similar in the two conditions, and, undoubtedly, in some stages at all events, definite distinction may not be possible (Virchow, Targett, and others). It is in the early periods that a clear and fundamental difference will be found. Virchow shewed that in osteo-arthritis the affection of the bones is secondary, and that the true seat of the disease is in the articular cartilage (*vide* Vol. III. p. 31). Now there are strong reasons for believing that in the trophic affections of joints the seat of the disease is in the bone, and that any change in the cartilage is subsidiary. A trophic affection of joints is always accompanied by a trophic affection of bones, and it can hardly be a mere coincidence that in the two diseases, tabes



and syringomyelia, which practically constitute the sphere of trophic arthropathies, the osteopathies should form an almost equally prominent feature; or that the bone and joint lesions should, in a large proportion of cases, appear in the same individual, in the same limb, and even in the same part of the limb. In the tabetic foot, which is a combination of bone and joint lesions, all the evidence goes to shew that the primary change is in the bone, and the same is true of the analogous vertebral lesions. If this is accepted, it is highly improbable that elsewhere an arthropathy should start from the cartilage. The conclusion is irresistible that in all cases alike the bone is the true seat of disease.

As to the atrophy—the rarefaction—of bone, which is regarded as the essential factor in the neuropathic joint, it is not its mere presence that is characteristic, for the *x*-rays have proved that it occurs in every prolonged or severe articular inflammation from whatever cause, but its early appearance and the degree that it may reach. In no other condition is a whole bone, such as a vertebra, the os calcis, or the astragalus, reduced to a pile of debris, or the upper end of the femur worn down to a point below the level of the trochanters. That the power of reaction is not lost is proved by the presence of osteophytes in the immediate neighbourhood. There are two ways in which such wasting of the bone may bring about changes in the joint of which it forms part; the one is by the occurrence of a spontaneous fracture on a considerable scale; it has, in fact, been argued that an arthropathy is simply a spontaneous fracture of an epiphysis (Rotter, Weizsäcker, and others), and there is ample evidence that this accident is not uncommon. In two instances the head of the tibia in an arthropathic knee which had been resected was found to be the seat of multiple fractures (Rotter); in others the head of the femur has been found loose in the hip-joint; and in other cases, again, the fluid effused without warning into a joint has been proved to be blood (Brissaud). Short of such conclusive evidence as this, the following features, which are common to all nervous arthropathies, point very strongly in the same direction: the absolutely sudden onset of the joint mischief, its occurrence after a slight injury, and the detection of fragments of bone within the articulation at an early date (Tournier, Westphal). But very often the arthropathy does not begin in this sudden way, and there may be no history of injury. For such cases a more insidious mode of action must be conceived. There is still some internal injury, but it is on a small scale and is difficult to prove: perhaps the breaking off of a small bony process, or, without even this degree of trauma, the rarefactive process in the epiphysis extends to the articular cartilage and undermines it. Ziegler suggested this, though as a minor occurrence, in osteo-arthritis, and he illustrated its advance side by side with the change proceeding from above. The cartilage thus undermined shews proliferation of its cells and undergoes erosion as in osteo-arthritis, while the exposed bone may either present compensatory change in the form of eburnation (this very rarely), or more commonly may collapse altogether. The rough similarity in certain phases of the



evolution of a nervous arthropathy and of osteo-arthritis is easily explicable on the supposition that the vicious circle described above is, *mutatis mutandis*, the same in both, that is, that in the one the disease takes the cartilage as its starting-point, in the other the bone. To sum up, in spite of certain characters common to other diseases of joints, particularly osteo-arthritis, Charcot's disease is a condition *sui generis*, and its essential factor is an atrophy of bone which specially affects the portion entering into the composition of the joint.

But it may be argued that analgesia alone is sufficient to account for the disorganisation of the joints. If analgesia were the effective cause, the marvel would be that any tabetic should escape, for analgesia of the deeper tissues is one of the most characteristic and common features of tabes. We should expect, moreover, that with progressive interference with afferent paths which marks the course of the disease the tendency to arthropathies would increase. But this is notoriously not the case; not only are arthropathies not unduly frequent in the later stages of tabes, but they occur most characteristically as an early symptom; so often, in fact, do they precede the earliest sign of disease of the nervous system that when this becomes apparent it is sometimes regarded as an instance of "traumatic tabes" or "traumatic syringomyelia."

The true explanation of this initiatory trophic change in the bone is not sensory paralysis but sensory irritation. Many years ago Dr. T. Buzzard drew attention to the frequency of the various visceral crises in cases of tabetic arthropathy. This observation was the first expression of a truth which has since obtained general recognition—that the bone and joint lesions of tabes, and probably of syringomyelia, are to be classed amongst the phenomena of irritation and not of paralysis. Brissaud systematised the same conception in his description of two forms of tabes, the one sensory, the other locomotor. In the sensory type the predominant symptoms are visceral crises, lightning pains, and affections of bones and joints; optic atrophy is an important member of the group, but does not concern us here. Brissaud went so far as to say that he had never seen an arthropathy in pure motor tabes. In syringomyelia, again, the subjects of arthropathies are frequently those who have pain; and, as pointed out, pain may be felt for long periods in a joint or bone which subsequently becomes the seat of disease. Finally, it is noteworthy that in Friedreich's disease, with all its similarities to tabes, no trophic affections of bones or joints are met with, and simultaneously the other phenomena of irritation cease to appear. There seems ample justification then, clinically, for regarding the osseous change underlying this group of nervous arthropathies as connected with irritation of nerves or nervous centres, and we may now consider the means by which this result is brought about.

An instructive parallel is provided by the familiar atrophy of muscles in connexion with injury or inflammation of an adjacent joint. The rapidity of its onset makes it impossible to explain this atrophy by disuse (Sudeck (78), Tedesko); and the persistence of a normal electrical reaction in the affected muscles proves that the atrophy is different from that

which occurs on a division of the motor nerve, is not, in fact, a primary degeneration. Many years ago Raymond and Onanoff shewed that the reaction was of the nature of a reflex; they set up a suppurative inflammation in two corresponding joints in a rabbit, having previously divided the posterior nerve-roots on one side only. The muscular atrophy appeared as usual on the one side, but remained absent on the side on which the posterior roots had been divided. The experiment has been repeated since by Hoffa with the same result. Skiagraphy has now shewn that in these circumstances a reflex atrophy of the bone is induced at the same time and in the same way as the reflex atrophy of muscle (Sudeck (78), Kienböck). It consists of a rarefaction of both the cancellous and compact bony tissues, and extends far beyond the actual vicinity of the joint. There is special significance in the fact that this change in the bones is also found quite apart from any joint-lesion in cases of injury of peripheral nerves, which are of a partial nature and associated with persistent irritation; such cases have been described by J. Ogle, Goldscheider, and Hirsch. Severe and persistent, though not necessarily continuous, pain is almost invariable in these traumatic cases, and vasomotor disturbance is nearly as common: the clinical picture presented is frequently that described as "glossy skin" (*vide* p. 82).

The correspondence between these traumatic lesions and those produced by disease is practically complete. The only possible conclusion is that the irritation, of which the lightning pains in tabes or syringomyelia are the evidence, constitutes an internal trauma as efficient in causing reflex atrophy as those external ones which have been taken as illustrations. One difference, however, should be borne in mind in the comparison between central and peripheral irritating lesions; though pain must be regarded as in all probability an essential concomitant of peripheral irritation, it is not so when the centres themselves are concerned. There is every reason to believe that in syringomyelia, for example, irritation may affect vasomotor and possibly trophic nervous elements without giving rise to painful sensations.

As to the afferent path of the reflex are there is no doubt; it consists of the fibres which subserve all forms of deep sensation and in some cases also those of protopathic sensation. With regard to the efferent track, there were formerly difficulties in accounting for the passage of efferent impulses by the posterior roots, but these have been cleared up by Dr. Bayliss's discovery that efferent vasomotor impulses normally travel antidromically by afferent fibres (p. 80). The question that still remains to be solved is as to the nature of these efferent impulses. Are they vasomotor or are they trophic? In answering this much will depend upon the sense in which the term vasomotor is accepted. If it is to be confined to changes in the calibre of the vessels, this explanation is beset with many difficulties. The first and most obvious is that the condition of the neuropathic bones and joints is so variable, so far as obvious hyperaemia or anaemia is concerned, that no conclusions one way or another can be based upon it. The second is the immediate juxta-

position in the neuropathic joint of tissues which are, on the one hand, atrophic, on the other hyperplastic; it is hard to imagine that this divergent condition can be brought about by either vasomotor spasm or paralysis. But if the term vasomotor be extended so as to include not only alterations in calibre but in the conditions which govern the exchange of fluid between the blood and the tissues, then the difficulties disappear. This wider view of the vasomotor function will make intelligible not only the undoubted association which exists between vasomotor and trophic conditions, but also such phenomena as the sudden development of oedema in the joint itself and in the surrounding tissues without any apparent change in the condition of the circulation. In Chareot's disease this remarkable association is found at least as frequently as any apparent hyperaemia or anaemia, and no explanation is worthy of the name which ignores it.

The reflex arc, then, is constituted of afferent fibres subserving deep sensation, efferent fibres of vasomotor type, and of a centre in the spinal cord of which nothing is known that would differentiate it from the vasomotor centres which occur at every level of the grey matter. As to the exact nature of the interferences which bring about trophic lesions it is not easy to dogmatise. Reasons already given for considering them mainly of an irritative nature need not be recapitulated. Probably mere interruption of afferent impulses is not in itself sufficient to set up trophic disturbance, provided that the function of the part is not interfered with. The tissues, however, are constantly on the brink of a precipice, and the activity which is necessary for their nutrition brings with it dangers which may lead to their destruction. The irritative influences may come into play at any part of the arc. Their method of action has been ably discussed by Goldscheider, whose suggestion, summarised in a few words, is something as follows: Appealing to Edinger's doctrine, according to which every exercise of function involves a lesion of the tissue except in so far as it is immediately repaired, he regards an internal irritation as eliciting the dissimilative part of the process while the reparative remains in abeyance. The level of the sensory tract responsible for these joint lesions is that of the sensory arc corresponding to the level of the trophic change. Thus in tabes, with its preponderating incidence upon the lumbar cord, the arthropathies are most commonly in the lower extremities, whereas in syringomyelia, which has a predilection for the cervico-dorsal region, they are mainly in the upper limb. This fact finally negatives the conception of a controlling trophic centre in the medulla which was originally made by Dr. T. Buzzard and has been more recently revived by Gibert.

The conclusions as to the causation of the osteopathies and arthropathies in both tabes and syringomyelia may be summarised as follows:—(1) The fundamental change is the same in both, and consists of an atrophy of bone. (2) This is a true trophic lesion to be distinguished from that due to disuse. It is produced reflexly by irritation in the course of a nervous arc, and is strictly analogous to arthritic atrophy of



muscle. (3) The general type which is assumed by an arthropathy is determined by local causes. The hyperplastic element, in particular, is to be regarded as in the circumstances a normal reaction to chronic trauma; but it is possible that in its degree it may express some derangement of nervous control which may be either irritative or paralytic.

## PART II.—OTHER FORMS OF TROPHIC OSTEOPATHIES AND ARTHROPATHIES

It is impossible to enter upon a description of the trophic lesions other than those which have already been considered without a strong sense of the difficulty and uncertainty of the subject. The osteo-arthropathies of tabes and syringomyelia are, as we have seen, peculiarly characteristic in themselves, and the spinal diseases with which they are connected are hardly less so; those which follow are to a large extent indistinguishable from other and ordinary affections, and their claims to a nervous parentage extend to every portion of the cerebrospinal system. As regards the bones, the chief difficulty arises from the paralysis with which the trophic defect is almost invariably associated, and which may bring about morbid changes as the result of disuse alone. It is equally difficult in considering the arthropathies to separate the changes which may occur in the joints of a paralysed limb as a form of neurotrophism from those which may result from an ordinary rheumatoid affection. Without regarding these difficulties as insuperable—for they certainly are not so in all cases—it must be recognised that a very rigorous investigation is necessary. There can be no question of adopting a neurotrophic conception as a matter of course, or as part of a general hypothesis. In this somewhat chaotic group the lesions which follow injuries or disease of the peripheral nerves stand on the firmest basis, and will be dealt with first.

### Trophic Affections following Lesions of the Peripheral Nerves.—

Experimental section of nerves in animals has given most contradictory results; and even where changes in the bone have been found (J. Ogle and others), the conditions have been so complicated by open sores or paralysis, or both, that no conclusions can safely be drawn from them. Even on the questions if the eventual result is an alteration in the size of the bone, and if so, whether in the direction of lengthening or shortening, experimenters are in complete disagreement (Nasse, Ghillini, Schiff).

(a) *Changes in the Bones.*—It is fairly certain that division of a nerve *per se* does not produce changes in the bone, except in so far as it causes paralysis. It is the partial division of nerves resulting in prolonged irritation that is the effective cause, and this, as we have seen, may be brought about by interference in any part of the reflex arc. Had x-rays been available Weir Mitchell would undoubtedly have completed his account of “glossy skin” by a description of the accompanying atrophy of bone. However interesting pathologically, the clinical importance of



atrophy occurring in these circumstances is obviously slight; but in rare instances a peripheral nerve lesion gives rise to bony changes of such a character as to be of clinical interest (Goldscheider, Hirsch, Blum, and others). These cases shew a progressive osseous atrophy leading to mutilation, such as is seen occasionally in syringomyelia even apart from ulceration. In a case of Berent's the pressure of a subclavian aneurysm caused acute osseous atrophy of this type. To the question if it is possible to distinguish the true neuritic atrophy of bone from that due to disuse, the answer must be a guarded affirmative. The distinctions laid down are as follows: (α) The onset is far more rapid than is ever the case from disuse alone; Nonne observed it four weeks after the lesion, and Köhler, describes it as often occurring within eight weeks after a nerve injury. (β) The degree of atrophy is more extreme than that due to disuse. According to Köhler, in a stump two years after amputation there was less atrophy of bone than can be found in the acute neuritic form in a few weeks. (γ) The texture of the bone is said to differ (Köhler), and is described thus: "The spongy portion shews a characteristic mottled appearance. In spots where there should normally be bony trabeculae there are gaps in the architecture. The trabeculae which still remain have indefinite washed-out contours; soon, even the cortical layer begins to shew tiny patches." (δ) The lime salts are disproportionately reduced, according to Exner, by 67 per cent, though whether this is not another mode of expressing the degree of atrophy is doubtful. Without impugning the accuracy of the observations, it will be felt by most that the differential diagnosis may be based with greater certainty on the general features of the case rather than upon minute differences in anatomical structure.

Spontaneous fracture occurs in leprosy as the result of changes in the bone which may be divided into three forms—(i.) Pure neuritic atrophy, such as is met with in both tabes and syringomyelia; (ii.) atrophy due to invasion of the medulla by leprous granulomatous tissue (Sawtschenko); and (iii.) necrosis in connexion with infection from ulceration of the superficial tissues.

(b) *Changes in the Joints.*—These are met with in the presence of irritative lesions, exactly as was found to be the case with the bones. Probably from the distribution of the nerve injuries, the small joints of the hand and foot tend specially to be implicated. There is some divergence of opinion both as to the character of the articular lesions and their frequency. Chipault, for example, maintains that changes in the joints are an almost constant result of injuries to peripheral nerves. Most writers, however, though holding different views as to their nature, agree as to their comparative rarity. Weir Mitchell describes the following condition as not uncommon:—"We may then have one articulation—and if only one, a large one—involved; or perhaps all the joints of a finger, or every joint of a hand, or of the entire limb may suffer. The swelling is never very great, the redness usually slight, and the tenderness on touch or motion exquisite. This condition of things remains with

little change for weeks or months, and then slowly declines, leaving the joints stiff, enlarged, and somewhat sensitive, especially as to movement. A small proportion of such cases find ready relief; but in many the resulting ankylosis proves utterly unconquerable, so that it is vain to try to restore mobility by manipulation or splints." Mr. Bowlby (8), on the other hand, considers these cases rare; he has never seen any so acute or painful. The articular lesions which he has met with are of a more chronic and less severe kind; in his experience at a period of from one to six weeks after an injury (to the nerve) the joints are usually somewhat stiff, but not painful. Occasionally, however, there is pain, tenderness, and swelling. The terminal condition is one of fibrous ankylosis. He compares the whole process to that of rheumatoid arthritis.

The anatomical changes are, in the first stage, effusion into the synovial cavity with hyperaemia of the synovial membrane; in the second, dryness of the synovial cavity, adhesion of the synovial pouches, and shortening with infiltration of the capsule and the surrounding structures; in the last stage the condition is one of false ankylosis from progressive contraction of the capsule, muscles, and ligaments which embrace the joint. In rare cases true fibrous ankylosis may take place from the extension of the synovial membrane over the surface of the cartilage, with fibrous metaplasia of this structure; but this, when it does occur, is found only after prolonged periods. It must be admitted that there is little to distinguish these changes from those which may be produced by an ordinary subacute rheumatism; and considering the frequent occurrence of this disease, or congeries of diseases, the danger of mistaking the *post hoc* for the *propter hoc* is considerable. In a case of injury to the ulnar nerve, which came under my observation, severe pains were complained of in the joints of the affected hand, and it appeared as if atrophic arthritis were in progress; but the appearance of the same symptoms in the corresponding articulations of the opposite side soon cast doubt upon the direct connexion of the articular with the neuritic lesion.

Very rarely injury to or irritation of a nerve may be followed by a fulminating arthritis of one or more of the larger joints. In Packard's classical case arthropathies of the knee and foot followed compression of the sciatic nerve by a tumour. Chipault found destructive arthritis of the elbow in a patient whose brachial plexus was compressed by callus formed in connexion with a broken clavicle.

The question of a true Charcot's arthropathy in leprosy has been the subject of much discussion; it is denied by some writers (Chipault, Londe and Perrey) and maintained by others (Hansen and Looft). On the whole, the weight of evidence is in favour of its presence. Hansen says: "Heiberg has described a foot which resembles the *pieal tabétique*. According to Heiberg, these leprosy trophic joint affections are characterised by swelling and laxness of the capsule of the joint, and wearing away and atrophy of the ends of the bones, or periostitis

ossificans, and hypertrophy of the ends of the bones, which is especially seen in the tarsal and metatarsal joints. We have been able to confirm these results of Heiberg, and have also seen, in such an ankle, growth of the synovial membrane with villous projections; the capsule of the ankle-joint was loose and lax, the talus smooth and oblique, and the cartilage worn away; and marked outward subluxation of the foot was present." Babes conclusively settles the matter both by his description and the illustrations of the tabetic foot, of various arthropathies, and of pure osseous atrophy. The occurrence of true Charcot's joints in leprosy is of considerable importance, for it is the only disease of the peripheral nerves in which they are found. The explanation lies, to some extent, in the extreme chronicity of the disease, but mainly in the analgesia of the deep tissues which is combined with unimpaired muscular power precisely as in tabes and syringomyelia.

**Trophic Affections following Lesions of the Spinal Cord** (exclusive of tabes and syringomyelia).—(a) *Of Bones*.—One lesion of the cord in this relation—*anterior poliomyelitis*—calls for special attention, and presents many difficulties. As is well known, pronounced atrophic changes in the bones occur in that form of it which underlies the disease infantile paralysis. It was long thought that this afforded convincing proof that the seat of the trophic centre for the skeleton lay in the anterior horns. Under the influence of this belief Charcot sought in these structures for the explanation of the osseous lesions in tabes. The comparative rarity of these bony changes in anterior poliomyelitis in the adult practically negatives this hypothesis. It seems clear that to a very large extent, at all events, the atrophy of bone associated with infantile paralysis depends upon the practical destruction of the muscles at an early stage of growth; the bone, deprived of the normal stimulus which it should receive from the stress and strain of its muscular attachments, and starved of its blood-supply by the lack of muscular action, fails to develop. But all cases cannot be explained in this way. Four weeks after the onset of acute poliomyelitis affecting the anterior tibial and peroneal regions in a boy of ten, Nonne found marked atrophy in the bones of the foot as well as the tibia. He also records 2 cases of chronic poliomyelitis with extreme osseous atrophy; in one of them the condition was associated with "glossy skin." We must recognise in addition to the relative atrophy of non-development when the disease affects a child and the positive atrophy from paralysis in the adult, an acute form which is a true neuropathy. This probably depends upon the irritation of vasomotor or trophic centres in the cord, as in the case of "glossy skin" just mentioned. Clinical observation shows that anterior poliomyelitis frequently oversteps its systemic boundaries, and may present all gradations up to a transverse myelitis, and it is particularly in these atypical cases that bony change has been discovered.

The same condition of acute atrophy has, as might be expected, been found in other lesions of the cord. From the paralysis which is generally present it can rarely reveal itself by spontaneous fracture, though some



examples of this are on record (Rivington); in some of these cases the dependence of the bony change upon the spinal lesion seems clear, for the limbs presenting spontaneous fracture, though not under the influence of the will, were in a state of active spasm, and their general nutrition was excellent.

(b) *Of Joints*.—In 1831 J. K. Mitchell recorded instances of arthropathies following Pott's disease of the spine; and Gull published a similar series in 1858. In 1859 Magnier described the same sequel in acute myelitis, and other writers have followed him. It is possible, however, that in some of these cases the joint was infected by the organism responsible for the inflammation in the cord. In the large majority the primary affection of the cord is either an injury, such as a stab, or compression. Arthropathies have occurred in progressive muscular atrophy (Proust and Étienne), and in amyotrophie lateral sclerosis; but they are extremely rare, and, unless reported fairly recently, are valueless on account of the probable confusion with syringomyelia.

The distribution of the articular lesions differs from that seen as a sequence of injuries to peripheral nerves in that the larger joints are attacked in preference to the smaller. The character of the arthritis is not essentially different, though there is perhaps a greater tendency to free effusion of fluid. There may be a subacute inflammation with pain and redness, or a painless arthritis to which attention is attracted only by accident. Rarely definite destruction of the joint occurs, as in Riedel's patient, who, it is important to note, was still able to walk; eight days after the injury—a stab between the first and second lumbar vertebrae—the knee-joint is said to have been disorganised. In another exceptional instance a fracture of the cervical spine was followed by hæmorrhagic effusions into all the joints on the paralysed right side (Alexandrini). In a case of fracture of the tenth dorsal vertebra both knees and ankles were distended on the fifth day with a considerable amount of sterile fluid; the ligaments were stretched and the cartilage eroded, but there was not any osseous change (Chipault).

**Trophic Affections following Lesions of the Brain.**—(a) *Of Bones*.

A true neuropathy of the bones has been rarely observed in connexion with various focal lesions of the brain, but the instances are of a most anomalous nature. An example in point is the hemiplegic patient described by Dejerine and Theohari. She suffered intense pain in the limbs, and the nerves were extremely tender. It is very doubtful if the condition of the bones is to be credited to the cerebral lesion whatever that may have been.

Fragility of bones leading to spontaneous fracture is comparatively frequent in all forms of chronic insanity. In most cases this depends upon an atrophic change which is to be attributed not so much to a local derangement of nervous influences as to a general lowering of nutrition. In dementia paralytica, however, the tabetic element complicates the situation, and we have in consequence to recognise the occurrence of spontaneous fractures of the two types—(a) those which are truly trophic



but due to concurrent tabes; and (b) those which are not trophic, but depend on a lowering of nutrition, which the bones share with the rest of the body.

These changes in the bones would appear to be those of pure atrophy with its associated decalcification; they are specially common in the ribs, but may affect the whole skeleton from the skull downwards. The fractures are often extremely numerous, and have attracted particular attention on account of their medico-legal importance (J. Ogle, Crichton-Browne, Neumann, Gudden). Besides this form of atrophy which results in spontaneous fracture, a condition of undue softness of the bones, leading to deformation, particularly of the thorax, has been repeatedly observed in the insane (Lähr, Meyer), but whether this should be classed under (a) or (b) is by no means clear. No general rules can be laid down which will decide the pathology of every case; except perhaps that if arthropathies coexist, the probabilities are strongly in favour of a neuropathic origin.

(b) *Of Joints*.—Arthritis in hemiplegia was first mentioned by Scott Alison in an article in the *Lancet* in 1847. Chareot reported cases in 1868, Hitzig several more in 1869, and since then there have been scattered publications on the same subject.

Neither the nature, the position, nor the severity of the cerebral disease appears to be a determining factor in the production of arthropathies; so little influence has the amount of paralysis that in one case, reported by Koschewnikow, aphasia was the only paralytic symptom. Hitzig remarks that the arthropathy frequently affects the less paralysed limb, and that the slighter forms of hemiplegia are more liable to it than the more severe. With regard to the former of these observations, it is remarkable that the shoulder is the articulation almost invariably affected, whereas in hemiplegia the arm, as a rule, shews more paralysis than the leg. In all Hitzig's 7 cases there were signs of vasomotor disturbance, as shewn by increase of local temperature and oedema. The arthropathy never occurred before the fourth week, and seemed often to be precipitated by the patient leaving his bed. The implicated joints were excessively tender, and on manipulation loud crepitus was heard. Hitzig rightly ascribes the arthritis to local causes, mainly to the paralytic subluxation of the head of the humerus, and compares it to the changes set up by prolonged fixation of a limb.

In the few available necropsies (Chareot, Hitzig, Koschewnikow) the morbid changes have always been those of acute or subacute synovitis. Effusion has commonly been absent, and the synovial membrane has shewn villous overgrowth and hyperaemia. The peripheral nerves and the nerve-roots have been healthy.

*Etiology*.—Little remains to be said on this point save to notice the atmosphere of doubt by which the hypothesis of an immediate nervous origin for those articular lesions is surrounded. The complete absence of any relation between the characters of the brain affection and the occurrence of an arthropathy seems almost in itself to disprove a direct

causal connexion. The majority of the patients are at an advanced period of life, when the joints are particularly liable to degenerative changes under any condition which entails disuse or even diminished function. Disuse implies lessened blood-supply, and in consequence the nutrition of the already impoverished tissue suffers still further. The improbabilities of an interpretation based on the existence of a cerebral nutritive centre are obvious; a trophic centre which is coextensive with the whole brain is self-condemned.

Space will permit but a passing reference to the possibilities of neurotrophic disturbance in certain diseases mostly of obscure pathology. Osteomalacia seems sometimes hardly compatible with any other than a nervous origin. It has been observed in several cases of the rare condition known as neuro-fibromatosis, and has then been limited to the bones of the trunk (Marie and Couvelaire, Haushalter). It has also been found in association with syringomyelia, probably as a trophic symptom of that disease (Moses, Sehlesinger), and may occur in connexion with various forms of insanity (Crichton-Browne). The osseous changes of osteitis deformans have been connected with degenerations of the spinal cord, but on insufficient grounds (Gilles de la Tourette and Marinesco, Leopold Lévi); the same claim has been made for acromegaly, and in fact for most diseases of uncertain pathology. But it is useless to deal further with mere speculations.

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## RAYNAUD'S DISEASE

SYNONYMS.—*Local Syncope ; Local Asphyxia ; Symmetrical Gangrene.*

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**Definition.**—Raynaud's disease comprehends three clinical groups of cases ; namely, local syncope, local asphyxia, and symmetrical gangrene ; and these three groups have the following features in common, namely : —(a) a temporary but recurrent morbid alteration in the blood-supply, and in the consequent nutrition of the extremities, and in some instances also of certain internal structures ; (b) circulatory and nutritive changes generally affecting similar parts on the two sides, though the changes are not necessarily equal in extent on both, and, exceptionally, the final manifestation may even be unilateral ; (c) a spasmodic and recurrent contraction of the arterioles—as is generally maintained—supplying the parts concerned and causing the morbid changes. It is also maintained that there is no primary organic change in the walls or lumen of the blood-vessels adequate to explain these results.

**Historical Note.**—Maurice Raynaud published his thesis on local asphyxia and symmetrical gangrene of the extremities in 1862 ; and in 1874 his final contribution on this subject appeared (45).

Before Raynaud's time there had been a frank recognition of many cases of spontaneous gangrene in which no tangible occlusion of blood-vessels, either from thrombosis or embolism, could be established ; obscure examples, arising as complications of typhoid and other exanthems, and in various morbid blood-states, such as diabetes, had been recorded, and suggestions had even been made that lesions of the nervous system might play a part in the causation of some of these cases. But Raynaud gathered together observations on simple phenomena like "dead fingers" ; on cases of recurring attacks of paroxysmal blueness of the extremities ; and, finally, on examples of limited benign forms of superficial gangrene ; in all of which symmetry was a marked feature. He shewed how these three groups of symptoms were associated, and that the gangrene was often the final outcome of the other two. His contention was that the one feature common and essential to these three morbid states is a spasmodic and frequently recurrent contraction of the arterioles supplying the extremities concerned. Since Raynaud's final contribution, there have been several additions to knowledge more or less cognate to his subject ; and in some directions new researches, especially on peripheral neuritis and obliterative angiitis, may somewhat modify the interpretation of some of the cases which he would have included ; on the other hand, certain observations have widened the scope of his original contention. It would appear best in this article to summarise the views of Raynaud, as originally stated by him, and then



to shew how far they require modification. The physiological basis on which it may be said that Raynaud's disease rests is the change which takes place on the surface of the body, and especially at its extremities, as the result of temporary exposure to cold. Local syncope has its analogue in the condition of simple pallor which is the result of contraction of all the surface vessels concerned, and which leaves the superficial tissues exsanguine. In the temporary blueness or cyanosis of the surface, which may also result from exposure to cold, there is contraction of the arteries with partial venous stasis—and this is the analogue of local asphyxia. In both these conditions we assume the contraction of the vessels to be a reflex act; the result of a sensory excitation of the cutaneous nerves, and an efferent impulse from the vasomotor centre in the cord determining contraction of the walls of the arterioles. The nearest analogue to the symmetrical gangrene with which we are concerned is frost-bite, in which a limited death of end-structures is the result of prolonged or rapid exposure to severe cold, whereby the blood-supply is suddenly arrested.

**LOCAL SYNCOPE.**—The simplest form of this morbid state is the phenomenon commonly known as “dead fingers.” In such an attack complete pallor of corresponding fingers of the two hands occurs rather suddenly. The index or little finger of each hand may be solely affected; or more than one finger of each hand may suffer: when this is the case the invasion of the other fingers may be either contemporaneous or progressive; and if progressive the same order is generally maintained. Much less commonly the whole hands up to the wrists, or indeed the lower part of each forearm also, become involved. The toes and feet may suffer likewise, either separately or contemporaneously with the upper extremities.

In the mild cases there is only slight discomfort in connexion with the attack, namely, during the pallid stage, a little pain which is compared to cramp; but the chief complaint is of a slight difficulty in the performance of small movements. The patient may be unable to grasp, or sew, or pick up small objects; and in like manner some slight difficulty may be experienced in straightening the toes. The extremities look thin and tapering, and the finger-tips are occasionally wrinkled, as in the algid stage of cholera. The surface temperature is lowered, and there is generally some modification of sensation. Of these modifications analgesia is most common; but the tactile sense is blunted, although the difference between heat and cold is still appreciable. The radial pulse is frequently unaltered, but in some recorded cases it became small and scarcely perceptible; it is in the small arteries and arterioles, as a rule, that the important alteration occurs; that there is temporary abeyance of the blood-current is shewn by the absence, in severe cases, of bleeding when the affected extremity is punctured with a lancet.

The duration of the attack varies between wide limits; it may last

but a few minutes, or, in severe cases, several hours. In the mild cases there is little to mark the end of the attack beyond the return to normal temperature, colour, mobility, and bulk of the extremity concerned; but in the severe cases the reaction is attended with burning pain. The arterial pulsations become very manifest (especially if the pulse has been feeble in the pallid stage), the extremities become hot, and the skin of a dull-red colour. There is then great intolerance of pressure and a craving for cold applications or exposure to cold air. During the stage of reaction perspiration sometimes occurs on parts of the extremities affected.

Recurrence of the attacks of local syncope is often very regular. Thus in the simplest form of "dead fingers" the subject of the complaint expects the familiar phenomenon before, during, or after the morning bath; and it only vanishes with the morning meal.

More severe forms of the affection, which disable for a time and render the sufferer a virtual invalid, often occur in a cycle of two or three months' duration; during which period an attack may set in regularly at a given hour in the day. So striking is this periodicity that the suggestion of malarial origin is not surprising. But it is noteworthy, with respect to these cycles, that there is not only a recurrence at about the same hour, but also a daily increase in the number and severity of the attacks; then a gradual diminution in number down to a vanishing point, when immunity returns for a varying interval.

It is astonishing how little constitutional disturbance may accompany these attacks, except some degree of exhaustion dependent on the pain and, in bad cases, on the sleeplessness. The general nutrition often suffers remarkably little.

Local syncope is more common in the colder than in the warmer months of the year. Attacks, mild or severe, are often precipitated by exposure to cold air or cold water; but in one of the cycles of the severe form of the affection the most insignificant difference—as, for example, passing from one room to the other—may determine an attack; and the occurrence of a chilly day in the middle of warm weather may start a cycle of attacks. Yet lowering of the surrounding temperature is but one of the determining factors: a certain number of those who suffer from the malady in its mild form experience it, with or without a general feeling of chilliness, during the period which succeeds the taking of a full meal. Such persons are often the subjects of slow digestion; nevertheless the liability to mild attacks of this kind is quite compatible with considerable bodily vigour and endurance.

Raynaud was inclined to lay stress on the neurotic side of local syncope; and it is undoubted that the severe forms are more commonly met with in women than in men, and especially in those who manifest hysterical phenomena. Certain recorded cases appear to have been initiated by a violent emotion, and others by trauma in a way precisely analogous with what occurs in some functional paralyses. Amongst the multiform manifestations of neurasthenia attacks of local syncope are by no means uncommon.

In one case the malady supervened on a condition of exhaustion after severe diarrhoea and prolonged "nursing." Mental distress and fag have also been recorded as antecedents. When cancerous cachexia has become established attacks of local syncope often supervene. There is no very obvious relation to menstruation, though in some cases the attacks have coincided with amenorrhoea. One woman found that her liability to attacks of local syncope completely disappeared with the commencements of her successive pregnancies. Although generally symmetrical, there are rare cases in which local syncope is predominantly and, perhaps, exclusively one-sided; a notable example of this kind is recorded by Graves. Even in such cases, however, if care be taken to observe the attack throughout, a lesser degree of the affection on the side apparently healthy may often be found, either preceding or succeeding the chief manifestation.

The ultimate prognosis of the mild cases is not grave. The affection is regarded by the person subject to it as a sort of habit of the circulation which he accepts or ignores. As already stated, moderately severe cases with their neurotic accompaniments often go through a cycle with gradual increase in frequency and severity of the paroxysms, and then subside and ultimately disappear. But there are rare cases of local syncope in which the paroxysms gradually lengthen, till at last, though there are exacerbations, there is scarcely any true interval; these cases sometimes end in terminal gangrene. Such cases will be considered hereafter, and likewise the treatment of local syncope in general.

**LOCAL ASPHYXIA.**—Local asphyxia, in common with local syncope, has these characters—that it is an affection of the extremities of the body; that the attacks are paroxysmal and recurrent; and that there is symmetry in the parts attacked. Raynaud was inclined indeed to regard it as a later stage of local syncope. An attack may begin, after exposure to cold water or cold air, with pallor of the affected extremities; but this initial pallor is frequently of very short duration, so short that the observer may fail to see it, the first really striking feature being the sudden appearance of duskiness of the skin of the affected parts.

A simple characteristic case which affects both hands and forearms affords the best opportunity of watching a paroxysm from beginning to end. There are a good many variations in the series; but either the whole hand becomes dusky, or certain fingers are picked out, the colour-change beginning at the tips and advancing proximally. The march of the paroxysm may be from finger to finger; then gradually the hand becomes invaded up to the wrist and, with lessening severity, along the greater part of the forearm up to the elbow, but rarely above it. The fingers of both hands may be affected simultaneously, though not to an equal degree. Sometimes one hand becomes affected first, and a definite interval of time elapses before the attack begins in the other. The colour varies within considerable limits; purplish-red, slate-blue, indigo, and the colour of blue-black ink are tints which are often noted.

The nails become extremely dark from the subjacent colour-change



in the matrix ; and, when individual fingers are picked out, the contrast with those not affected is very striking.

Simultaneously the affected parts become extremely cold to the touch. In one of Raynaud's cases there was a difference of fifteen degrees between the temperature of the palm and that of the axilla. The pain is, as a rule, much more severe than that of local syncope, and often makes the patient moan or scream. Throughout a prolonged attack there are decided remissions and exacerbations, suggesting alternating and varying spasms of vessels with varying effect on nerve-endings. Pressure of any kind is often unbearable. The tactile sense is diminished, but, on account of the pain and restlessness, it is very difficult to test it. There may be analgesia to a superficial pin-prick, but by a deep prick pain is elicited. There is recognition of the difference between heat and cold, and cold is often preferred to heat. The patient may be unable to grasp small bodies, such as a pin ; and there is some temporary difficulty in the performance of the finger movements. The veins on the back of the hand, wrist, and forearm shew marked distension as the general blueness of the surface increases up to its maximum ; and a curious livid marbling along the sides of the veins is often to be seen on the proximal side of the limit of the deep coloration. In one case, which I observed during the march of the paroxysm, portions of the veins on the back of the hand became quite moniliform ; that is to say, there was an alternation of small dark swellings with narrow, almost colourless, intervals between them. While under observation the dark swellings gradually altered their position along the course of the veins, pointing to a varying contraction of the walls of these vessels. As with local syncope, the radial pulse may remain unchanged during the attack, or may become smaller in volume ; if the subsequent reaction be severe the pulse then becomes full. In some cases during the paroxysm a slight tumefaction of the fingers and of the back of the hand occurs, which is, in fact, a slight degree of oedema.

The area of temporary whiteness of skin, which can always be produced by firm pressure on a normal hand, remains obvious during the paroxysm for a much longer time than normal ; shewing the excessive slowness of capillary reaction in these cases.

As in attacks of local syncope, there may be a sudden outbreak of dew-like moisture over the whole hand near the end of the attack. The duration of a paroxysm may be from one to six or seven hours.

The subsidence of the paroxysm may be sudden ; more commonly it is gradual. The finger first affected generally leads the way in the return to normal colour ; but the change may start on the back of the hand instead of on the finger-tips. Islands of less deep blue appear, gradually unite, and by degrees replace the dark area ; but there are often curious remissions in this process, blue and red areas appearing alternately. Ultimately the whole extremity becomes deep red, and for a varying time feels quite hot ; sometimes the radial pulse becomes full. One finger-tip may remain blue for a time when the rest of the



hand is red ; but the oedema may continue for a couple of hours, or for half a day, or rarely for twenty-four hours after the paroxysm is over. This, however, is exceptional ; the early return to the normal state is the rule. The temperature in the mouth is often unaltered during a paroxysm ; but subsequently a very slight pyrexia may ensue. In a protracted case (that of a woman aged forty-five) under my own care the mouth temperature during an attack was sometimes normal ; sometimes  $97.6^{\circ}$  F. ; rarely a little above normal ( $99^{\circ}$  F.). In the evening after an attack, and sometimes next day, the temperature occasionally rose to  $100^{\circ}$  or  $101^{\circ}$  F.

In rare cases a little desquamation over the extremities of the digits occurs for a few days after a severe attack. During the colder months a paroxysm of the kind described may be induced, in one who is subject to such attacks, by going out of doors, or by putting the hands into cold water. But it may also be precipitated by some emotional disturbance ; in one case it occurred after a fright, and simultaneously with the sudden arrest of the menstrual flow. It may occur during convalescence after parturition, especially if the patient have been poorly fed or badly nourished. An attack of choleraic diarrhoea may determine it. As with local syncope, the attacks sometimes come in cycles ; and, during a cycle, going from one room to another, in which the temperature is a little lower, seems sometimes to induce an attack. Again, in summer weather a sudden drop of temperature seems likewise, in a predisposed person, to determine an attack. But when a cycle is established the attacks are apt to begin at the same hour for several successive days, independently of any obvious determining cause. Also, they gradually increase in frequency or duration, or both, so that several occur in the same day : then, by degrees the attacks become less frequent and less severe, till they come to a vanishing point ; and once more the patient has immunity for a longer or shorter interval.

In those who are liable to attacks of local asphyxia there is considerable variation both as to frequency and duration. A single solitary attack may occur, or a cycle may last for a few days, or for a week, or for two months. The more severe cycles last from two months up to ten months ; but in them, as well as in some of the shorter cases, symmetrical gangrene frequently occurs, a condition which will be discussed separately. The foregoing may be taken as the description of the simplest form of local asphyxia as it affects the upper limbs ; but it is to be noted that other parts may be affected in like manner. Thus, the lower limbs are attacked at least as often as the upper, and corresponding toes are often picked out ; the local asphyxia sometimes extends to the heels, above each ankle, or even up to the knees. The alteration of sensation is not so marked in the feet as in the hands. Occasionally during the attack the patient is unable to recognise the nature of the surface on which he stands ; or, when the attack is fairly established, even to stand at all ; in one case, however, under my own care, some impending attacks were warded off by prolonged and vigorous walks. In some instances all four extremities suffer, either simultaneously or in

succession. Raynaud points out that in persons who suffer from attacks which vary at different times in respect to the number of extremities affected, the severity, as measured by the degree of cyanosis and pain, is greater when two extremities are affected than when four are affected. Also (as in local syncope), though symmetry is observed, there is sometimes great inequality in the incidence of the affection on the two sides; so that at certain stages it may be described as unilateral.

The helix of the ear may suffer, either simultaneously with the feet or hands or, in some cases, without the invasion of these members. In rare cases the nose is affected. The zygomatic regions may also suffer, and occasionally the nates and the front of the thighs. When the areas of local asphyxia in the same individual are multiple, some of them may be almost painless.

Reddish-purple round, or oval, areas on the limbs sometimes appear in proximity to the sites of the local asphyxia. They may be raised and painful, presenting some resemblance to erythema papulatum or to erythema nodosum; but they sometimes affect the deeper layers of the skin also, present no obvious elevation, and give rise to no pain. The latter form is persistent for many weeks, and leaves enormous pigmented patches behind it. It is more common in the cases which go on to gangrene; occasionally indeed these "*tachetéés*" (as they have been called by French writers) become themselves the site of a limited gangrene, as in one of Southey's cases. Possibly the cases described by Cavafy as symmetrical congestive mottling may be milder examples of the same condition.

With respect to deeper structures the occasional occurrence of slight oedema has already been mentioned. This oedema may continue for half a day, or rarely twenty-four hours after the subsidence of the paroxysm.

Raynaud observes that in some of his cases there was fibrous ankylosis of terminal phalangeal articulations, and some thickening along the processes of the palmar fascia, which persisted between the paroxysms but ultimately vanished with the other signs of the disease. I have notes of a case with the same association and the same sequence.

**SYMMETRICAL GANGRENE.**—Raynaud described local syncope, local asphyxia, and symmetrical gangrene as three successive stages of the same malady. In a broad way this series may be accepted, but it requires a little qualification: for, in some cases, gangrene supervenes upon attacks of recurring cyanosis of the extremities; in others the dominant character is local syncope, in which the fingers are subject to paroxysms of pallor, bloodlessness, and pain; and by degrees these conditions become almost constant, the digits assuming a more and more parchment-like and tapering appearance, and gangrene supervening rather suddenly, without any definite intermediate attacks of local asphyxia (*vide* Fig. 20). In both forms the glacial coldness of the extremities becomes very pronounced and continuous, and the pain is almost unbearable. Small bullae may form first on one extremity, then on another; the bulla breaks and gives exit







## PLATE I.

Foot in case of Raynaud's disease. Drawing made during attack of local asphyxia.

Girl aged 5 years. Attacks began when  $3\frac{1}{2}$  years old, in the month of February. She had been carried out in somebody's arms, and at the time was wearing woollen stockings and boots. When brought in to the house she complained of cold. The feet were blue, and the blueness extended up to the ankles; it lasted for seven hours. She vomited, but nothing else remarkable was observed. Next day she played as usual. From this time she was liable to repeated attacks in the winter after exposure, but also in the house if she sat about much. The attacks did not occur while the child was in bed.

In a typical seizure one foot becomes suddenly blue, beginning at the toes, extending to the ankle. The veins on the dorsum and lower part of the leg are slightly distended. Both feet suffer, but to an unequal degree, one foot being attacked a little later than the other. Both feet are stone-cold. In other attacks the hands and forearms are affected as well as the feet.

Distension of the veins of the dorsum of the hand and of the forearm is very striking. In one attack varying contraction of the veins was obvious to the naked eye. Dark knotty swellings appeared with almost colourless intervals between them. The knotty swellings altered their position along the course of the veins during the progress of the paroxysm.

During the paroxysms the radial pulse is only just perceptible. Between the attacks there is no indication of any alteration of the arteries whatever. The pain begins with the onset of the blueness. During the earlier and middle stages of the attack, the child screams when the hand or foot is touched. During the later stage she is often lethargic. When the attack is subsiding, mottled areas of less intense blueness become manifest in the middle of the dorsum of the hand and foot; successive digits become less blue; ultimately the extremity becomes pink and to the observer's hand feels hotter than natural. The attacks observed in hospital were seldom longer than two hours' duration; occasionally they lasted only half an hour. The body temperature (axilla and rectum) was normal in some of the attacks, but rose a little in the evening and on the next day ( $100^{\circ}\text{F}$ . and  $101.2^{\circ}$ ). Haemoglobinuria was not present. The child was observed during several winters. No sign of vascular or nervous disorder appeared. She derived great benefit from galvanic treatment during the paroxysms.



FIG. 20.

Case of symmetrical gangrene of tip of both index-fingers following attacks of local syncope.

The patient, a delicate lady in poor circumstances, had suffered much trouble. When first seen in May 1885 she was forty-four years old. The only point of importance in her history was that fourteen years previously she had lived in Mauritius for four years, and suffered severely from ague. During the last thirteen years she had lived at an English seaside place, and there was no evidence that she had had any distinct malarial attack.

During the previous winter she had suffered from dead fingers on rising, some fingers being worse than others. At these times she had the usual clumsiness of local syncope and was unable to close her fingers. Later on in the day she could sew, knit, and play the piano as usual. The tip of the tongue and the lips felt numb during cold weather, and in a cold wind she complained that her lips became so stiff that she could hardly speak.

She was a pale, pinched, poorly nourished woman with some pigmentation of the

face. The lips, nose, and ears were thin and waxy looking, and the finger-ends tapering, pale, and cold, with a very slight blue tint at the extremities.

There were no gross vascular signs, and no signs of peripheral or central nervous disease. The viscera were normal and the urine was natural. In the beginning of December she appeared again, having been comfortable during the summer, but with the onset of the cold weather her symptoms had returned in an aggravated form. The fingers as before were thin, pale, and tapering, and very slight contraction was beginning to appear at the terminal joints. The extremity of the left index-finger was in a state of gangrene. Two-thirds of the palmar surface between the tip and the normal transverse groove were black and mummified, and on the dorsal surface a groove was forming round the nail, but only the distal half of the matrix was black. The gangrene was almost dry and was free from any smell of decomposition. (The drawing was made a fortnight later, when the granulating margin of the line of demarcation had become obvious.) There was no anaesthesia except at the extreme tip. The slight atrophy of the hand was general; there was no picking out of any group of muscles.

The radial arteries were well and equally felt; they were not at all tortuous and did not roll under the finger. They were perhaps small, but the patient was a small woman and had small limbs.

The right hand resembled the left in every respect except the gangrene; but this began to threaten, sixteen days subsequently, in an identically similar spot on the tip of the right index-finger. The progress of the gangrene was like that of the left finger. Although by the end of two months the pain had ceased, six months had elapsed before the cicatrisation was complete. There was no separation of bone, and the ultimate appearance of the fingers was as though the extreme tips had been cut off with a knife, leaving, however, the proximal half of the matrix of the nail, so that a small nail was reproduced.

Although the gangrene had not been averted, the patient's general nutrition, as well as the nutrition of her extremities, had been greatly improved by galvanism, shampooing, Turkish baths, rest, and nourishing food. She continued these remedies with gradually lessening zeal, and got through the next winter without any recurrence of gangrene. But next spring she shewed some thin scaly areas over all the projecting points of her upper extremities, and the hands felt cold, dry, and a little stiff and horny. Dry scaly areas appeared also on the margins of the ears, and now the chest-walls began to shew the hidebound condition of sclerodermia. This gradually increased, and next year she died. The details of her last illness were not obtained beyond that she became progressively marasmic.

to a little blood-stained fluid ; it then collapses, and a small black epidermic layer covers the area, which becomes gangrenous. The process is generally definitive in the sense that the extent of the gangrene is limited, or nearly limited, by the boundary of the small area on which the bulla forms. The blackened epidermic layer forms the top of a hard, thickened eschar ; around this arises a zone of ulceration which leads to the gradual separation of the sequestrum of skin. The bed of the nail is often involved, and the nail separates, either wholly or in part ; and a new nail grows which may be somewhat deformed. Though the gangrenous process may extend down to the bone it is quite exceptional for any necrosis of the bone to take place. The scar which is left after complete cicatrisation may indeed be very small, but the tip of the affected finger remains tapering in form. In some cases the process is even more benign than this. No bulla forms, but the extremity shews a gradual mummification, and a small blackened area slowly separates by a quiet ulceration, leaving exceedingly little deformity.

The process of gangrene may affect several finger-tips, or only a single finger-tip on the two hands. The affection may be either simultaneous or successive.

When the toes are affected the lesions are often confined to the plantar surface, and the separation of the sequestrum of skin is more quickly effected than in the fingers ; the nails frequently escape, and the toes do not present the tapering shape which is so characteristic of the affection of the fingers. Some months subsequently, on examining the plantar surface of toes which have been attacked with this form of gangrene, the only abnormalities found are small white scars, such as might have resulted from cutting away a small slice of the true skin.

Raynaud speaks of the nose and external ears being threatened, but he had not seen mortification of these parts. Sir J. Hutchinson has recorded a case in which small sloughs occurred on the tip of the nose, and one on the helix. A definite loss of the substance of some part of the margin of the helix occurred, several times, in two cases of local asphyxia under my care. One is delineated in figure 21.

Besides the benign chronic characteristic cases which have been described there are others of which Raynaud quotes some exceptional examples in which the spontaneous gangrene is acute, severe, and progressive, affecting extensive portions of the extremities from below upwards as far as the wrists, elbows, ankles, or knees. Other examples have been recorded by Sir Thomas Smith (1880) and by Mr. W. G. Spencer (1892). These cases generally seem to be determined by cold, though the degree of cold does not appear to be necessarily excessive. There are likewise some cases of chronic Raynaud's disease which become continuous, and give rise to a severe form of gangrene in which the ultimate pathological changes are very different from those in the benign cases (*vide* p. 143).

**Diagnosis.**—From the pallor of chlorosis local syncope is distinguished





FIG. 21.

Ear of a man, aged thirty, who was the subject of Raynaud's disease with recurrent attacks of symmetrical gangrene. On the helix, antihelix, and in the fossa between them, there is a surface to a considerable extent black and gangrenous, with a sharp-cut edge and a few scanty granulations from which there is some bleeding. The other ear is not so severely attacked, but shews signs of past loss of substance and a recent thin black edge of gangrene and some indolent granulations. There is some patchy pigmentation of the cheeks.

The man had lived at the Cape for a few years, and "while working his way up country" had suffered for three weeks from what was considered a malarial illness. In December 1885 he came home by a long sea-route, and when sailing round Cape Horn he felt the cold severely, and suffered from burning pain at the edge of both ears. Then a black spot appeared, which was followed by some loss of substance. Every winter since then he has been liable to burning attacks, followed ultimately by black areas of gangrene on the edge of each ear.

His vulnerable time is from November to April. Since his return to England he has had three attacks of what is assumed to be ague with definite shivers; each attack has lasted two days. Otherwise his health has been good. He says that on some occasions he has passed dark urine. That which was examined at the time of one of the gangrenous attacks did not shew any trace of haemoglobin or of albumin.

The edge of the spleen could not be felt.

by its being a local and paroxysmal rather than a general and persistent condition.

Local asphyxia cannot be distinguished from the effect produced in a solitary instance by frost-bite or exposure to extreme cold. We are rather concerned with a recurrent paroxysmal habit of the circulation, the phenomena of which are often determined by an insignificant lowering of temperature, or even by a mere emotional disturbance. From the signs in the extremities which characterise a case of congenital heart disease it is easy to distinguish those which belong to local asphyxia; the blueness of the extremities in a case of *morbus caeruleus* is an exaggeration of the general cyanotic colour of the body; but, moreover, there is a marked clubbing or bulbous condition of the finger-ends, the toes, and the nose. In local asphyxia there is no general blueness; the lips and tongue are remarkably free from this change of colour; the finger-ends are either tapering or, in rare cases, the seat of a temporary oedema, and they are seldom clubbed, or but slightly so: furthermore, the intermittency of the blueness of the extremities is characteristic. When Raynaud's first observations were published, peripheral neuritis had not been studied with the complete methods of pathological and clinical research which have subsequently been brought to bear upon it; but Raynaud pointed out that the anaesthesia and the paresis of local asphyxia are too transient to be the outcome of primary and permanent changes of nerve-trunks and their branches; and that the pains of local asphyxia and of its later phase, symmetrical gangrene, are not propagated along recognised nerve-paths. Local asphyxia is often confounded with chilblains; but in the latter the more or less circumscribed areas of dull-red colour are generally situated at some little distance from the very ends of the digits affected; they are somewhat swollen, they present some degree of actual inflammatory exudation, and, although they come and go, their duration is not paroxysmal: in all these respects they differ from areas of local asphyxia. Symmetrical gangrene, in its proneness to mummification, resembles some of the quiet forms of senile gangrene; but it differs in several ways. (i.) As to distribution: senile gangrene is limited to a single limb, or, if it affect more than one limb, the lesions are successive in order. The lower limbs are more frequently affected than the upper; whilst in symmetrical gangrene, as the name indicates, corresponding extremities are attacked simultaneously, and the upper limbs quite as commonly as the lower. (ii.) As to extent: symmetrical gangrene is typically limited to the skin and the subcutaneous structures, whilst senile gangrene is generally more profound, either affecting a whole toe or a great part of the foot. (iii.) As to progress: symmetrical gangrene is more definitive than senile gangrene. It frequently attacks the extremities of several toes on both sides at once, or after a short interval; these become superficially gangrenous in isolated spots, and the gangrene does not extend beyond the areas at first invaded. Senile gangrene, on the other hand, tends to be serpiginous; it begins at a single point, and spreads to an indeterminate extent. (iv.) As to the state of the arteries:

in senile gangrene there are generally indications of arteriosclerosis; the vessels supplying the limb are cord-like, and often the arterial pulsation in them is much diminished, or even obliterated. In symmetrical gangrene of Raynaud's type no alteration of the arterial walls can be detected, and the arterial pulsations are generally quite distinct. (v.) As to the age of the patient: in symmetrical gangrene many of the cases have occurred in quite young persons, even in children, subjects in whom the factor of arterial degeneration, in the ordinary sense, does not arise.

In respect to the embolic origin of certain cases of gangrene it may be pointed out that such cases differ from Raynaud's disease in that they are rarely symmetrical, and that a source of emboli may be found either in damaged cardiac valves or in cardiac thrombi. Nevertheless Raynaud, amongst rare contributory causes of symmetrical gangrene, admits valvular defects, and congenital narrowing of the aorta and of the systemic arteries. I have had under my own care one example in a child, the subject of cardiac disease with great enfeeblement of the systemic circulation, in whom local asphyxia and limited symmetrical gangrene of fingers of Raynaud's type appeared, and in whom the necropsy failed to yield evidence of embolic obstruction; such cases are, however, very rare.

Phlebitis, when it leads to gangrene, gives rise to the moist form of this lesion; and not to the limited symmetrical manifestations with which we are now concerned.

As a rule, it may be taken that there is no naked-eye change in the heart or large vessels to explain the phenomena of the symmetrical gangrene of Raynaud's form.

In diabetic gangrene we have either a lesion which is primarily traumatic or inflammatory, and which runs on to acute rapid necrosis; or one in which premature arterial change, or trophic nerve disturbance, plays an important part.

Raynaud's disease bears some resemblance to ergotism. Although we have a large mass of detailed statement concerning the toxic effects of ergot in the way of gangrene, yet the anatomical descriptions of the arteries in fatal cases are singularly meagre. Raynaud made several attempts to estimate the effects of toxic doses of ergot on some of the lower animals, but failed to obtain any results in the least comparable with the form of symmetrical gangrene with which we are concerned. In two of his clinical cases rye-flour had been used for a time in the diet, but there was no evidence that the rye was infected. Another case was that of a woman who was confined in November, and in February began to suffer from local asphyxia, which was ultimately succeeded by gangrene of the finger-tips; this patient had taken a gram and a half of ergot during her labour, but the interval between this and the appearance of the symptoms of local asphyxia was surely too long for us to suppose that the drug had played any part in their production. In the other cases ergot, as a possible factor, could be excluded with tolerable confidence. Raynaud's disease must be distinguished from multiple neurotic gangrene of the skin and



from gangrene produced by the application of carbolic acid or potash to the extremities (40).

**Nosological Affinities.**—The most interesting of the later observations lead to a wider conception of the morbid processes concerned, and first amongst these comes Raynaud's own discovery that occasional *temporary alterations in the fundus oculi* alternate or coincide with manifestations of local asphyxia in the extremities.

In his last memoir Raynaud relates the case of a man, aged fifty-nine, with no relevant antecedent, except intermittent fever thirty-five years previously, who in the month of December began to suffer from local asphyxia of the fingers of one hand, and in the next month of the fingers of the other hand; then the feet were affected, and then disturbances of vision set in: when he came under observation he had very cold hands and indurations of the flexor tendons; and he exhibited intermittent attacks of local asphyxia on going out into the air or on bathing his hands in cold water. The feet were affected likewise, but less severely. The heart was normal, the radial pulse and the pulse in the posterior tibials and arteries of the feet were perfectly perceptible, and the arteries were not indurated. The eyesight was good in both eyes during the attack; but during the period which followed, and while the fingers were returning to their normal colour, the sight, especially that of the left eye, became dimmed—to recover, however, at the onset of a new attack. Ophthalmoscopic examination of the left eye during a period of reaction,—that is to say, when the cyanotic colour of the extremities was at its minimum,—shewed that “the central artery of the retina and its branches had very clear contours, and that they were definitely narrower round the papilla than at the periphery; here and there was a sort of partial constriction, the papilla was very clear; the veins were the seat of remarkable pulsations a little later than the radial pulse. . . . The central vein dilated and elongated itself so notably in the region of the papilla as to simulate a small aneurysm, but the pulsation was also visible in the smaller veins.” In the right eye there were similar phenomena, but less well marked. The ophthalmoscopic examinations were verified by Galezowski. Under a course of electrical treatment (*vide* p. 146) the patient recovered from the local asphyxia of the extremities, and also from his visual troubles; finally, the ophthalmoscopic examination revealed nothing abnormal. The second case was in a young man, aged twenty-two, with diabetes insipidus. He had local asphyxia of the upper extremities, and also some blueness of the face; his attacks, which were more common in the early morning, became well marked when he went out into the air, the blue regions of the skin becoming excessively cold. During the attacks the radial pulse was very small. “At the commencement of the cyanosis the patient complained of a notable obscuration of sight, which disappeared when the face and hands returned to their natural colour.” Panas observed that at the beginning of the cyanotic attack the “arteries of the fundus oculi were definitely narrowed,” and that “when reaction occurred they became widened.” “The retinal veins were turgid, but



presented no appreciable pulsation." In the striking case of symmetrical gangrene of the fingers recorded by Weiss, there was considerable generalisation of these processes; for not only were there extensive transitory changes in the joints (*vide* p. 139), but also remarkable ocular phenomena, referred by him to the cervical sympathetic. As in Raynaud's first case of amblyopia, these phenomena occurred in attacks which alternated with some of the seizures of the extremities. For several days the patient had "retraction of one eyeball, narrowing of the palpebral fissure, contraction of the pupil with no reaction to light, and a slight degree of ptosis. . . . At the same time there was reddening of the zygomatic region and of the external ear of the same side, some elevation of temperature, and hyperidrosis. . . . As this attack subsided there was a little superficial gangrene of the skin of the zygomatic region in the shape of some small patches of first brown and then blackened epidermis, which ultimately separated." There were several attacks of this kind affecting the left side of the face and left ear, and some affecting the right side, and at times both simultaneously; but only on the left side were the eye phenomena well marked. Weiss thought that the eye phenomena depended on ischaemia of the cilio-spinal region of the cord. In a case of Sir Jonathan Hutchinson's, mentioned in the next paragraph, there was iridoplegia on the left side: the pupils were large and unequal, the left being bigger than the right, and they were motionless, both to light and accommodation; they contracted under the use of Calabar bean. The vision was good.

With regard to the generalisation of the malady, the next observation of importance is that of the occasional association of *haemoglobinuria* with Raynaud's disease. It is strange, indeed, that Raynaud should never have noticed this connexion. The first suggestion of it is found in the history of a case recorded by Sir J. Hutchinson as far back as 1871. A woman, aged thirty, had suffered during the winter from frequent shivering fits after exposure to cold; these attacks were accompanied or followed by general malaise, and the urine often became dark after them. One cold day, after returning home, her nose and left ear were found to be quite black, and small superficial sloughs gradually separated from these spots; but during her stay in the hospital no blood was noticed in the urine. The patient also had iridoplegia. Robert Druitt, in 1873, in recording his own case, maintained that he suffered from "obvious ague attacks, and also from distinct attacks of haematuria related to cold, exposure, and worry." He describes these attacks as being associated with "numbness, tingling, and blueness of the extremities, the blue patches being at times suggestive of imminent gangrene." In 1879 Sir S. Wilks recorded the case of a patient, aged sixteen, who had profuse suppuration from the bursa between the gluteus maximus and the great trochanter, which had followed some injury to the hip. When under Sir S. Wilks's care he was cyanotic in certain regions, and there was a systolic murmur at the third right space. The margins of the ears, the nose, and the toes became very blue; and the tips of the thumbs and of several fingers

became affected with gangrene, from which they slowly recovered. The urine was often dark in colour and gave the guaiacum test. Debris and granular casts were present, but blood-corpuscles could not be found on several occasions; at a later period, however, some blood-corpuscles were present (*vide* Vol. IV. Part I. p. 541). Southey, in 1880, described a case of symmetrical gangrene of the legs, and local asphyxia of the fingers, of Raynaud's type; a trace of albumin was noted in the urine, but there is no record of the presence of haemoglobin. The history of the patient shewed that she had passed black urine with some of the attacks in which the fingers became numb, black, and dead. In Southey's second case of local asphyxia and symmetrical gangrene (1883) intermittent haematuria occurred on several days after exposure to cold. The "blood was usually very apparent by its dark colour and the obvious sediment that it gave, but its presence was at times only detectable by the guaiacum reaction." Oxaluria usually either preceded or accompanied the haematuria. There seems little doubt that the case was one of haemoglobinuria. In 1883 I recorded three cases of Raynaud's disease, in one of which there was typical haemoglobinuria. I then pointed out the marked parallelism between cases of intermittent haemoglobinuria and characteristic cases of Raynaud's disease—those, that is to say, in which the local asphyxia is paroxysmal, with return to a normal state between the attacks. Neither are truly periodic, but both are paroxysmal; and in both affections the attacks have a remarkable relation to changes of temperature. By far the greater number of cases of both affections occur in winter or cold weather, if not exclusively at any rate primarily; and when the warmer weather appears, if the attacks do not vanish they notably diminish. In both the attacks may be accompanied by some abdominal pain and slight pyrexia; both may be followed next day by sleepiness, and by a certain sallowness of complexion and of the conjunctivae. It is rare for intermittent haemoglobinuria to occur when the patient is in bed, and this exemption is also observed in many typical paroxysmal cases of Raynaud's disease. I suggested that possibly other visceral paroxysmal affections might be found, in these conjoined cases, comparable with the temporary enlargement of the spleen sometimes found in haemoglobinuria. This suggestion I have verified in a case under my care; a young man was subject in cold weather to typical attacks of local asphyxia of the four extremities and of the ears, with recurrent gangrene of the margins of the helix on both sides. Some of these attacks were associated with haemoglobinuria, and with enlargement of the spleen and slight pyrexia, followed on the next day by a little yellowness of the conjunctivae and sallowness of the skin. The question of malaria was considered, as the man had lived for a time in a malarial district; but the most careful examination of the blood during the paroxysms failed to identify the malarial parasite.

Dr. Dickinson is even more sweeping in his identification of these two diseases. He holds that the two conditions "seem so to approach each other and mingle as to make it impossible to make a distinct demarcation

between them." The most striking case narrated by Dr. Dickinson as bearing on this point was that of a girl who was under observation in the hospital for typical attacks of intermittent haemoglobinuria. On one occasion her usual attack was replaced by an attack of paroxysmal local asphyxia affecting one hand, unattended by the usual alterations of the urine. Dr. J. Abererombie (1886) recorded a case of a boy who was liable to attacks of local asphyxia affecting the hands, legs, cheeks, and ears; and who in some of his attacks passed urine with sp. gr. 1023, which contained one-tenth of albumin, gave the guaiacum reaction, and shewed amorphous material and oxalates, but no blood-corpuscles. Dr. Abererombie suggested that paroxysmal haemoglobinuria and Raynaud's disease are of the same nature, and that the jaundice sometimes found after the attacks of haemoglobinuria is the result of arterial spasm of the hepatic vessels. This is a debatable doctrine; but there is much to be said in favour of the discoloration being due to haemolysis.

Some reference must be made to the observations on the blood in cases of intermittent haemoglobinuria. It is well known that, during an attack, blood drawn from a cold extremity shews marked changes in the corpuscles; they do not form rouleaux, they become extremely crenated, and granular masses appear in the serum. Murri maintains that corpuscular destruction occurs in the superficial vessels, and that arterial spasm is an essential factor. Boas found that corpuscular changes could be discovered in the blood from the finger of a certain patient, the subject of paroxysmal haemoglobinuria, if the finger were put into iced water. Fleischer blistered one of his haemoglobinuric patients during the inter-paroxysmal period, and found that after a paroxysm had occurred haemoglobin could be discovered in the serum of the blister. In the foregoing observations no special attention was directed to the question of local asphyxia of the extremities; but in 1885 A. T. Myers recorded a case which was singularly complete in this connexion. A boy, aged seven years, when recovering from measles, suffered for the first time from paroxysmal haemoglobinuria. The paroxysmal attacks were sometimes, but by no means always, accompanied by a slight rise of temperature (to about 100° F.) for a few hours; after the attacks there was slight but distinct icterus, lasting as a rule about twenty-four hours. The spleen was very slightly enlarged, but no definite temporary enlargement during the paroxysms was established. About the same time the ears became subject to attacks of coldness and blueness, and of aching as they became warm at the close of the paroxysms. Subsequently gangrene occurred on the margins of each ear; and there were several relapses, either of slight gangrene or of local asphyxia, during successive winters. The attacks of paroxysmal haemoglobinuria continued, being more frequent in winter than in summer. Blood withdrawn during these attacks from the cyanosed ears, and from the hands, shewed the following changes:—The coloured corpuscles shewed an abnormal disinclination to form rouleaux, sometimes had crenated edges, and sometimes were fairly normal in outline.



"Blood flakes" were found varying in colour from deep reddish-black to a thin transparent red, and in size from about four to ten times as large as a normal red corpuscle.

Drs. Colman and Taylor, in 1890, recorded a case of Raynaud's disease not associated with haemoglobinuria while under their observation, in which there were local changes in the blood. A girl, aged ten, had attacks of local syncope of the fingers of the right hand, and sometimes of the left as well, preceded by pain behind the sternum. The blood carefully drawn from the fingers during the attack presented the following changes: "There was distinct coloration of the liquor sanguinis, the tint of the film being about half the depth of that of a healthy blood-corpuscle, many of the red blood-corpuscles were shrivelled and irregular, the projections being much blunter and less regular in size and form than the crenations seen in specimens of blood that have been allowed to evaporate. . . . Some corpuscles were nearly normal in shape but quite colourless, whilst several were completely collapsed, and what appeared to be fissures could be seen in their walls. . . . The individual white blood-corpuscles were normal, but appeared to be relatively increased in number. There was no increase of haematoblasts, nor were there any blood-plates. . . . To check these observations blood was taken from an unaffected finger of the left hand, and also from the lobule of the ear. . . . These specimens were completely normal."

Mr. W. G. Spencer, in 1892, recorded the case of a boy, aged thirteen, who, after sleeping two nights, in the month of February, in a van, with two other boys, was brought to hospital with dry gangrene of the ungual phalanges of all the toes of the left foot, and of those of the second and third toes of the right foot. The two other boys did not suffer. Although it was stated that the circulation in the extremities had previously been good, yet inquiry elicited that, from the age of one year upwards, the boy had complained much of pain in the loins and between the shoulders whenever the weather was cold; and that upon these occasions he passed urine as dark as port wine. When the boy was brought the day was cold, and he passed some urine which was dark-coloured, gave the guaiacum reaction, but did not contain any red blood-corpuscles. Although this case is described as one of frost-bite, it seems fair to regard it as a case of Raynaud's disease with haemoglobinuria.

*The Skin.*—Urticaria (brought on by a chill) was noted by Southey during some of the paroxysms in one of his cases, and the same skin affection after exposure to cold has been recorded in paroxysmal haemoglobinuria (Dickinson, S. Mackenzie, and Forrest). Numerous recorded cases shew the connexion between Raynaud's disease and sclerodermia (*vide* p. 91). Ball, in 1871, reported the case of a woman who, for five years, during the winter, had suffered from hard yellowish patches on the extremities of the fingers, which subsided in the spring. She was liable to attacks, during which there was much pain, redness, ulceration, loss of substance, and tardy cicatrization at the tips of the fingers; the toes



were affected also. Ball recorded this as a new variety of sclerodermia ; but there was no trace of sclerodermia in other parts of the body, and the case was claimed by Raynaud as a chronic form of local asphyxia and symmetrical gangrene. Dr. Colcott Fox has mentioned that in two of his cases of sclerodermia, in which the hands were attacked, there had been for a long time a liability to dead fingers. "One of these cases continued to suffer from mild attacks of local asphyxia of the fingers after the onset of the sclerodermia." Finlayson recorded the case of a man, aged thirty-six, who had well-marked sclerodermia of hands, feet, legs, front of chest and abdomen, neck, and face. This patient was much influenced by exposure to cold, and ultimately suffered from gangrene of the fingers and toes, for which no sufficient explanation was forthcoming at the necropsy. I had under my own care a lady in whom the succession of events was the reverse of that which occurred in Finlayson's case. The patient had typical attacks of local syncope of the finger-ends, ending in symmetrical gangrene of the tip of each index-finger ; she recovered, but the fingers presented the atrophied, tapering, parchment-like character described by Raynaud, with very slight contractions of the last phalangeal joints ; she was subsequently attacked by extensive sclerodermia of the chest-walls, and died marasmic (*vide* p. 128).

*The Joints.*—Raynaud referred to fibrous ankylosis of the terminal phalangeal articulations, and to thickening along the processes of the palmar fascia ; and shewed how remarkably such thickening may clear up on recovery from local asphyxia. Prof. Wardrop Griffith has recorded three cases of Raynaud's disease in which marked contractions occurred, with limitation of movements and some shortening of muscles. Sir J. Hutchinson has described a group of cases which he calls "last joint arthritis" ; these he believes to be related to Raynaud's disease.

Sometimes the larger joints are affected ; in Southey's second case, during one of the attacks, effusion occurred in both knee-joints. Weiss (1882) has recorded a long series of observations on a case of symmetrical gangrene under his care. In the early attacks only the finger-joints suffered ; but in the later ones the left knee, the right elbow, the right shoulder, and the right wrist were affected. Weiss's summary is as follows:—"There was effusion in the joint cavities and infiltration of connective tissues above and below the joints ; once there was synovitis of the metacarpo-phalangeal joint of the right middle-finger followed by teno-synovitis of the flexor tendons of this finger. . . . On one occasion there was effusion into the knee-joint associated with exudation into the cellular tissue of the thigh and knee. Sometimes the joint effusion was preceded by pain, in other cases it was painless. . . . The swollen joints and the swelling of the soft parts were not specially tender to pressure. The skin was only reddened once, namely, in the case of effusion into the shoulder-joint ; the temperature was not raised at the outset, and the course was afebrile throughout. . . . In most cases absorption was rapid, and the constituent parts of the joints returned to the normal state." Weiss, accepting frankly the view of the central origin of

Raynaud's disease, was inclined to regard these joint affections as mild forms of an arthropathy dependent on some temporary change in the hypothetical joint centres of the cord.

*Cerebral Symptoms.*—Many of Raynaud's cases were of neurotic proclivity. One of them was admitted to the Salpêtrière with "epileptiform attacks and notable alteration of intelligence and incoherence of ideas." Dr. Monro lays stress on the occasional occurrence of convulsions in those who are the subjects of Raynaud's disease. Osler and Thomas record the case of a cabman, aged twenty-six years, who during several successive winters had attacks of Raynaud's disease, some of which were definitely associated with convulsions and unconsciousness. Other associated conditions were haemoglobinuria, colic, and splenic enlargement. In Southey's third case (1883), a boy aged nine, there were maniacal attacks in the early part of the illness, when gangrene of one finger-tip was already present. Probably the severity and long continuance of the painful attacks, especially in poorly fed marasmic subjects, may be responsible for a certain amount of temporary mental instability. A middle-aged woman, under my own care, during slight remissions of her attacks of local asphyxia, had recurrent headaches, and delusions which were always worse in the evenings, not unlike those of Korsakow's polyncuritic psychosis. Removal to an asylum was considered, but after a time she made a complete recovery. In another case of severe local asphyxia of the hands with threatened gangrene (in a young woman under my own care), marked chorea with maniacal delusions occurred. The late Dr. Southey informed me that, since the publication of his papers, he had seen many asylum cases "which presented manifestations of local asphyxia." During one phase of the illness in Weiss's case, ataxic aphasia, without paralysis of limbs, appeared. Prof. Osler records a case of Raynaud's disease with recurrent attacks of hemiplegia and aphasia.

*Spinal Cord and Peripheral Nerves.*—The advance of histological research since Raynaud's time has led to more detailed investigation of the nervous structures in cases of gangrene; but it is open to question whether some of the cases in which extensive changes of these structures have been found would have been admitted by Raynaud, on clinical grounds, as belonging to the groups defined by himself.

Pitres and Vaillard (1885) narrate two cases with extensive changes. The first was that of a young woman, aged twenty-four, of feeble intelligence from childhood, who at eighteen began to suffer from tremors and stiffness of the limbs with subsequent contracture and dementia. After a time the feet became cold, blue, and insensitive, and then gangrenous; the left foot undergoing spontaneous amputation, and the right becoming almost separated. Many eschars appeared in various parts of the body, some of which suppurated; and the patient died from exhaustion. On necropsy the tibial arteries were seen to terminate in a cicatricial cul-de-sac, which was surrounded by fleshy granulations. In no part of the arteries of the lower limbs were adherent thrombi found, but soft clots

only. The aorta and its branches and the veins of the limbs were healthy, and the viscera shewed nothing special. There was chronic hydrocephalus of the lateral ventricles, some adhesion of the pia mater to the cortex, and much thickening of the skull. There was a slight diffuse sclerosis affecting the whole of the antero-lateral columns and the greater part of the posterior columns in the dorso-lumbar region. The spinal ganglia and nerve-roots, so far as they were examined, were normal. "The nerve-trunks of the upper limbs and of the thighs were normal, the anterior and posterior tibials of both sides presented changes which were fairly symmetrical; these changes were extensive atrophy of nerve-fibres with empty sheaths presenting numerous nuclei, and at intervals varicose dilatations which contained masses of granular protoplasm and drops of myelin. . . . Between the fibres in many places there were leucocytes filled with small granules, and presenting the aspect of Gluge's corpuscles." In the second case—that of a woman aged fifty-six, who for six months suffered from inability to feel the ground on which she trod—bullae had formed on the soles of the feet two months before admission. Subsequently the feet became swollen, painful, and covered with reddish patches on the dorsal surface; fresh bullae formed, and there was complete anaesthesia over considerable areas of both feet. Gangrenous areas formed across the middle of the tarsus on both sides, and death followed from exhaustion. On neeropsy, neuritis of the plantar and tibial nerves was found; but the vessels of the limbs were normal, as also were the brain, spinal cord, and other viscera. Pitres and Vaillard met the objection that the neuritis might have been consecutive to the gangrenous process, by giving the results of an examination of the peripheral nerves in a case of embolic gangrene in which they found the nerves normal throughout. The only remark to be made about the above cases is that they did not conform or even approximate to the clinical type described by Raynaud; for example, in these cases there were extensive areas of persistent anaesthesia related to the neuritis, and possibly playing some part in the production of the gangrene.

Mountstein (quoted by Hochenegg, 1886) describes the case of a man, aged fifty-one, on whom amputation of the right leg in the upper third was performed on account of gangrene of the foot, which had begun two months before. The neeropsy shewed many calcareous plates in the posterior tibial artery, but no adherent thrombi. The small vessels close to the gangrenous focus had only minute thrombi in them. The posterior tibial nerve shewed interstitial neuritis, especially near the gangrenous area; and in the left (sound) lower limb similar changes were found in the posterior tibial nerve. Brain and cord were anaemic, and the examination of the viscera was negative. The clinical record is not adequate to shew that this was a case of Raynaud's disease.

Hochenegg (1886) reports a case of a man, aged fifty-one, who had gangrene of the left hand with no obvious vascular disease. The necropsy shewed chronic hydrocephalus and syringomyelia; there was but a slight degree of atrophy in the peripheral nerves, and this he



regarded as secondary to the cord lesion. Hochenegg held that the gangrene was caused by the central lesion.

Dr. Wiglesworth (1887) has recorded a case of extensive peripheral neuritis in a woman, aged twenty-six, who was the subject of epileptic dementia and of chronic Bright's disease. She had suffered from repeated attacks of spontaneous gangrene of the fingers and toes, and presented extensive atrophy of the muscles of both hands. The sciatic, internal popliteal, external popliteal, posterior tibial, median, and ulnar nerves on both sides, and the musculo-spiral on the right, were examined. Most of them shewed overgrowth of connective tissue, with atrophy and degeneration of nerve-elements. The spinal cord shewed only a slight general thickening of the neuroglia, and some alteration of the posterior vesicular columns of Clarke. Dr. Wiglesworth held that the gangrenous areas were dependent on the nerve-changes.

Dr. Affleck (1888) gives the results of the examination of the internal plantar nerve and the blood-vessels in a foot that was amputated for gangrene, which had followed attacks of pain and local asphyxia. The blood-vessels were normal, but the nerve shewed extensive neuritis.

Rakhmaninoff (1892) describes a case of disseminated multiple neuritis, in a young man aged seventeen, following an attack of typhus fever two years before the patient came under observation. There were coldness and numbness in the hands and feet, twitching in the muscles of the hand and forearm, severe pains in the limbs, in the chest, and in the abdomen, much hyperidrosis of the body, redness and swelling of the dorsum of each foot, extending up to the ankles, and the lower parts of the feet became livid blue. A line of demarcation formed round the ankles, and amputation had to be performed below the knees. At the necropsy, besides pleurisy, pneumonia, and splenic enlargement, thickening of the vessels of the limbs, with narrowing of the lumen, was demonstrated. There was also neuritis in the nerves of the upper and lower limbs, rather in the small branches than in the trunks.

A case is recorded by Dr. Handford (1890) of disseminated myositis and neuritis, probably of alcoholic origin, in which at one time there was limited dry gangrene of the tips of the thumb and index-finger. Although no necropsy was obtained, there could be no doubt about the neuritis; as there were extensive areas of persistent anaesthesia, and, besides remarkable thickenings and much atrophy of certain muscles. But the limited areas of gangrene supervened on a process of sudden acute oedematous swelling, which was quite unlike Raynaud's disease in its course.

Dr. Samuel West (1889) obtained a necropsy on a case of Raynaud's disease, in which there had been recurrent attacks of local syncope and local asphyxia of the hands and feet, and a purplish erythema of the face, which became blue and livid, especially at the tip of the nose and on the ears, when the attacks of blue fingers appeared. This purplish erythema was accompanied by a certain amount of branny desquamation. The patient died of an intercurrent pneumonia. On microscopic



examination the radial artery at the wrist and the median and the radial nerves were found to be normal. The spinal cord was normal.

For several years I had a man under observation who, in successive winters, presented typical Raynaud's disease in both feet. He had, first, attacks of local syncope in the left heel, subsequently in the toes, and then in corresponding parts of the other foot. He was able in part, and for a time, to ward off these attacks by sharp walking; and when the warmer weather came they diminished in frequency and severity. During the second winter the attacks assumed the character of local asphyxia of the toes, he presented blue patches (*tachetées*) on the thighs, and subsequently on the buttocks; and his finger-ends became very cold, but not blue. He then had a little gangrene limited to the tips of the second and third toes of the left foot. In the succeeding winter, when his paroxysmal attacks returned, he was greatly benefited by the daily vigorous galvanic treatment to be described on p. 146, and thus was enabled to resume his work. By the use of galvanism and shampooing during cold seasons he did well until the winter of 1886-87, four years after he had been first seen; then, he and his wife having become careless with regard to these measures, his malady gained upon him; the toes of both feet became very blue, and in the spring of 1887 gangrene became imminent in the left foot and rapidly extended to the ankle. There was suppuration, the patient became extremely exhausted, and amputation in the middle third of the thigh was accordingly performed. The patient made a good recovery. The stump was carefully examined in respect of nerves, arteries, and veins: the nerves were quite healthy, the arteries were free from calcification or atheroma, but there was a definite thickening of all three coats, and a remarkable contortion and infolding of the elastic lamina. The walls of the veins were also thickened. For two years the patient had no serious recurrence of vascular trouble, though he still suffered from local asphyxia of the right foot; then, rather suddenly, gangrene supervened in the right foot, but less severely than in the former attack. The right leg was likewise amputated in the middle third; the patient made a good recovery, and has been in moderate health since. There seems little doubt that this case was primarily one of Raynaud's disease. The attacks were paroxysmal; almost restricted to the cold weather; improved by going to bed; relieved by vigorous exercise, and almost cured by galvanism and shampooing: moreover, they were unaccompanied by clinical evidences of neuritis; that is to say, such atrophy as occurred was general, and did not pick out special groups of muscles. There was no reaction of degeneration, nor was there any persistent localised anaesthesia. As the attacks became very chronic the nutrition never really recovered between the paroxysms; and it would appear, in the light of the subsequent anatomical investigation, that the case approximated to one of obliterative arteritis (*vide* Vol. VI. p. 559). In this disease, as pointed out by Friedländer and Buerger, the veins undergo thickening and narrowing as well as the arteries. It seems reasonable to suppose that recurrent spasmodic

contractions of the vessels may ultimately bring about a permanent alteration in the walls and lumen.

*Relation to Diabetes.*—Dr. Colcott Fox narrates the case of a man, aged fifty-one, who suffered from local syncope and local asphyxia of the fingers, and threatenings of gangrene of one great toe; besides some symmetrical gangrenous sores over the junction of each middle and lower third of the shins. The man proved to be the subject of diabetes; and Dr. Fox mentions that only in one of Raynaud's reported cases was this disease present, and that the local asphyxia in that case preceded the first definite diabetic signs by eight years. It seems probable, with regard to symmetrical gangrene following upon paroxysmal attacks of local asphyxia, that the association of diabetes is accidental; in the benign form, at all events, the progress is quite different from diabetic gangrene as commonly observed.

*Relation to Malaria.*—Raynaud does not appear, in his early memoir, or in his "new researches," to have considered the possibility of any connexion between the disease which he described and malarial fever; but in two of his earlier cases (vi. and viii.) local asphyxia appeared a fortnight after an attack of tertian ague. The first patient described in his "new researches" had suffered from ague thirty years previously. In his article on gangrene (46) Raynaud says, that "although, after repeated attacks of intermittent fever, oedema of the limbs, with or without thrombosis, may often be observed, no examples are known of gangrene special to the malarial cachexia." This is far too sweeping a statement. Several cases of local syncope, local asphyxia, and gangrene have been recorded as occurring in persons who either were suffering from ague at the time, or had suffered from it. Petit and Verneuil (1883), in a complete review of the subject, describe different forms of gangrene. Some of them resemble the variety which has been found as a complication of different exanthems, and these are not strictly comparable with Raynaud's type. But there are others, indistinguishable from Raynaud's cases in that they occur in young subjects, are symmetrical, terminal, dry, and limited. It would seem, moreover, that in some cases, both of local asphyxia and of gangrene, there was some response to quinine. Mourson (1880) is inclined to place the local asphyxia of malarial subjects alongside some of the anomalous central and peripheral nerve affections which occur as sequels and "larval" forms of ague. In four cases of Raynaud's disease under my care there was a history that previous malarial attacks had occurred. In one of these (*vide* p. 136), during the paroxysms of local asphyxia, symmetrical gangrene, and haemoglobinuria, although the spleen was enlarged, no parasites could be found, and no benefit resulted from prolonged use of quinine and arsenic; in the other cases there appeared to be no other indication of active malaria at the time of the attacks; the only determining factor was cold. It seems possible, nevertheless, that ague may bring about some change in the economy, in consequence of which the vasomotor control or vasomotor resistance may be lessened, and the

influence of external cold become thereby a more powerful factor than in normal circumstances.

*Relation to Syphilis.*—Two of the patients recorded by Raynaud (Nos. xvi. and xvii.), one a man aged thirty-four and the other a woman aged forty-six, had suffered from acquired syphilis in an aggravated form. A remarkable case of symmetrical gangrene was described to me by Dr. H. Humphreys in a child who was the subject of congenital syphilis. Mr. F. Marsh also described a case of the same kind in a syphilitic boy. From the character of the permanent upper median incisors, in one case of local asphyxia under my own care, the patient was suspected to be the subject of hereditary syphilis. It is conceivable that syphilis might be a co-operating factor in determining the occurrence of gangrene of the extremities, by causing disease of the inner and middle coats of the smaller and middle-sized arteries. But there are so many cases of Raynaud's disease in which syphilis can be excluded, that it is obvious we can at best reckon it as one only amongst other favouring conditions.

*Relation to Obliterative Arteritis.*—This disease, first described by Friedländer, and more recently investigated by Dr. Parkes Weber (54) and Buerger (*vide* Vol. VI. p. 559), presents, when it affects the limbs, many features in common with Raynaud's disease. Local syncope and local asphyxia may certainly be induced; and there may be an entire absence of areas of anaesthesia or localised atrophy of muscles (thus separating it from peripheral neuritis); finally, gangrene of the dry mummified variety may supervene, and this may even be symmetrical (Pearce Gould). I am inclined to the opinion that some long-continued cases of Raynaud's disease, in which the paroxysmal phase has given place to persistent change, may, in their final stage, become examples of obliterative arteritis; a case under my own care (p. 143) seems to support this view. But it is most important to recognise that, in Raynaud's disease, the pulsations of the principal arteries of the limbs can be felt distinctly at the outset, and in most cases throughout; during the paroxysm the pulsation often diminishes, but in the inter-paroxysmal periods it is obvious.

**Summary.**—Pathological research has eliminated some of the chronic gangrenous cases from Raynaud's clinical groups. There can be no doubt about the occasional occurrence of multiple areas of gangrene in cases of peripheral neuritis, whether pure and simple, or associated with syringomyelia, Morvan's disease, or other central lesions. In these cases, when considering the causation of the gangrene, there is first the element of persistent and profound local anaesthesia to be reckoned with; and there is, also, the possibility of a concomitant obliterative disease of the arteries: for the experimental researches of Byvoets, Fraenkel, and others would seem to shew that damage to the main nerve-trunks of a limb may induce some degree of obliterative disease in the arteries of the limb. In other groups of cases there is the possibility that the principal arteries of a limb may be normal so far as clinical investigation reveals, but that the smaller vessels may become affected with obliterative disease.



There still remain, however, a large number of cases—(a) in which there are no areas of persistent anaesthesia; (b) in which there is no localised atrophy of groups of muscles; (c) in which the symptoms are paroxysmal with a return to the normal state in the inter-paroxysmal periods; (d) in which there is marked symmetry; (e) in which the arterial pulse, though narrowed during the attacks, becomes normal between the attacks; (f) in which the subjects are young and with no evidence of degenerative disease,—to which the title of Raynaud's disease is justly applied. Furthermore, when we consider the extension of some of these cases, the progress from one limb to another, and the occasional association of temporary amblyopia and haemoglobinuria, we are led to ascribe the symptoms primarily to a pathological habit. The easiest explanation of this pathological habit appears to be Raynaud's hypothesis; namely, that the vasomotor centre or centres are unduly irritable; that the commonest irritant is from the periphery, for example, cold; and that the efferent impulses from the centre lead to the paroxysmal contraction of arterioles.

**Treatment.**—In his last memoir Raynaud was led, by his view of the pathology of the disease, to try the effect of the continuous galvanic current. He employed the descending current down the spine, the positive pole being placed over the spinous process of the seventh cervical vertebra and the negative pole over the lumbar region. He used the sulphate of copper battery of Trouve and Onimus, beginning with twenty elements and progressively increasing up to sixty-four. The remarkable improvement which took place under daily applications of this treatment in the case of local asphyxia and alternating amblyopia (*vide* p. 134) led him to apply it in other cases. Raynaud, however, was soon led to place the electrodes locally over the affected limbs as well as down the spine.

I submit the following method as one which has proved useful in the galvanic treatment of these cases:—Immerse the extremity of the limb, which is the subject of local asphyxia, in a large basin containing salt and tepid water; one pole of a constant-current battery is placed in contact with the upper part of the limb, above the level of the water, and the other pole in the basin, thus converting the salt and water into an electrode. As many elements as the patient can comfortably bear should be employed; and the current should be made and broken at frequent intervals, so as to get repeated moderate contractions of the limb. The patient should also be instructed to make voluntary movements of the digits while the galvanism is applied. It will be found that in a typical paroxysmal case, if two limbs be similarly affected, the limb which is subjected to the above treatment will recover more rapidly than the one which is simply kept warm. In many cases during the acute phase of the attack shampooing is quite impossible; but if galvanism be first employed as above, it will then be found practicable to shampoo the limb; the painful spasm having been thus overcome.

In the chronic cases, although the relief is not so marked, galvanism



unquestionably improves the nutrition of the limb, and aids in withstanding imminent gangrene. The cases which do best are those in which galvanism, shampooing, and Swedish movements are employed daily. In bad cases all these measures may be used twice daily; or indeed whenever a paroxysm occurs. In severe cases Prof. Osler speaks highly of Cushing's method of applying a tourniquet for half a minute to the bandaged limb. Its application, which is painful, is followed by intense hyperaemia. Its action depends on the physiological "blocking" effect of the elastic constriction of the peripheral vasomotor nerves; as a result the terminal arterioles relax, and arterial hyperaemia takes the place of local asphyxia due to spasm. The diffusible stimulants and vaso-dilators, such as nitrite of amyl, nitroglycerin, and the like, have yielded little or no beneficial results, so far as my experience has gone. Alcohol relieves to a slight extent, but its employment is attended with the grave risk of inducing the inebriate habit. Opium is valuable when gangrene is threatened. Cannabis indica has been found helpful in a few cases. Hot applications are seldom useful. Southey found in one of his cases that an ice-bag applied over a painful extremity gave considerable relief. During convalescence Turkish baths, hot-air baths, or electric-light baths are very helpful; and a warm climate, with plenty of sunshine during the winter, is always to be sought for if feasible. Before exposure to cold, persons who are liable to Raynaud's disease should fortify themselves with nourishing food, and protect themselves by woollen clothing. Constipation and delayed digestion seem to play an accessory part in some of the attacks, and small doses of mercurials often appear to be helpful.

In gangrene of the benign form, simple protection, antiseptic precautions, and rest are all that are needed; severe cases should be treated on surgical principles. Experience indicates that the outlook of amputation is more hopeful than in cases of extensive atheroma or diabetes.

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## ERYTHROMELALGIA

SYNONYM.—*The Red Neuralgia.*

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**Definition.**—"Erythromelalgia is a chronic disease in which a part or parts of the body—usually one or more extremities—suffer with pain, flushing, and local fever, made far worse if the parts hang down."

**Historical Note.**—The above definition states in Weir Mitchell's own words his summary (1897) of the essential features of the malady which he first described in 1872, and named in 1878. So far back as 1843 Graves cautiously stated his opinion that the nerves and arteries of a part of the body could influence local circulation, independently of the heart; and he recorded 2 cases which conform to Weir Mitchell's type, and are quoted by Mitchell. Graves described another case, also quoted by Raynaud, which seems to lie half-way between the group of cases designated as "Local Syncope" and that now under consideration. In 1871 Sir James Paget gave an account of what may be called an intermediate case between these two groups. In Weir Mitchell's first paper exclusive attention was given to the lower limbs, and no better clinical picture of the disease can be given than as it occurs in a single foot. But in 1878 other examples were recorded by Weir Mitchell in which the hands also were affected; and some in which the hands were affected exclusively. Moreover, in the more generalised cases great variations of clinical phenomena were observed, which pointed to widespread organic or functional disease of the nervous system. With a wise reserve Weir Mitchell refused to attempt to declare the origin of the malady; though he inclined then to the view that it is due to spinal or cerebrospinal disorder, and that some distinct lesions of definite parts of the nervous system might ultimately be found.

Since the appearance of Lannois' thesis in 1880, the best synopses of the literature of the subject have been those of Lewin and Benda, and of Cassirer. Lewin and Benda in 1894 analysed 41 cases, and classified them under the three following groups: namely, (i.) those in which a true organic central nervous disease exists; (ii.) those in which the disease of the nervous centres is functional; (iii.) those in which the nervous disease, organic or functional, is only peripheral. In 1901 Cassirer collected 90 cases reported as erythromelalgia. For the most part the malady has been regarded as a vasomotor neurosis, or as a



vasomotor paralysis; but Weir Mitchell now rather ascribes it to peripheral neuritis; of this, however, there is as yet no conclusive anatomical proof. Moreover, the claim for erythromelalgia to be distinctly classified has been contested; it has been maintained that it should rather be designated as an unstable symptom-group which may be variably associated with many different diseases. However, the special symptoms described by Weir Mitchell occur sufficiently often, apart from any others, and are so uniformly grouped that they clearly deserve clinical definition and a name. The latest histological investigations (*vide* p. 153) seem to indicate that the clue to the pathology will be found, not in the cerebrospinal axis nor in the peripheral nerves, but in definite changes in the walls of the smaller arteries.

**Etiology.**—*Age.*—Out of Lewin and Benda's 41 cases the majority occurred in middle life. There are, however, a few young patients, namely, at the ages of sixteen, twenty, and twenty-one respectively. Baginsky records a case in a boy aged ten.

*Sex.*—Males are more often affected than females; of 41 cases 29 were male and 12 female.

*Occupation.*—It appears that long hours of standing, associated with heavy work and stress, and also exposure to varying temperatures, may play some part as determining causes. The following is a list of the trades followed by some of the victims of erythromelalgia: iron-worker, copper-polisher, alkali-worker (who stood for hours in front of a furnace, his hands being held in cold water for long periods), locomotive-driver, seaman, fisherman, postman, baker, waiter, collier (who worked in a coal-mine with his feet in two feet of water ten hours at a stretch), a poor Russian tailor, who worked ten to twelve hours daily at a sewing-machine in miserable surroundings. The disease is very apt to occur amongst poor Jews in New York (Buerger). Well-marked instances, however, are recorded of patients who were not subjected to any physical strain and who were in easy circumstances, but inquiry should always be made as to how far such patients have been exposed to considerable vicissitudes of temperature.

*Previous Health.*—The nervous constitution has been regarded as a predisposing factor; but although there are a few instances in which hysteria became manifest during the progress of the case, there are a considerable number in which it could be confidently excluded. The wearing pain, recurrent and then almost incessant and singularly refractory to treatment, is in itself adequate to induce lack of emotional control. Of the female cases, there is one of Eulenburg's (21), an anaemic young woman in whom erythromelalgia began soon after her confinement; in two other patients, namely, Graves', aged sixteen, and Stillé's, aged twenty-nine (reported by Weir Mitchell), the symptoms supervened upon cessation of the menses. In the first of these the cessation was associated with an exhausting diarrhoea; but in the second it was sudden, after falling into a river. In Weir Mitchell's first case the antecedents of prolonged erythromelalgia were insolation on the African coast followed by a



severe fever, which left behind it a weak heart with an apical systolic murmur. Another of his patients had had severe remittent fever; and he lays stress on the fact that this patient had used a geological hammer with great persistence. Enlenburg had 1 case in a patient who had suffered from severe malaria. J. Ross, quoting Elliotson, draws attention to gonorrhoea as being sometimes responsible for erythromelalgia, especially when radiating from the heel. Morgan gives 1 severe case which may support this view. The association with different forms of cerebrospinal affections mentioned on p. 160 might suggest syphilis as a remote factor in common to them. I have seen a mild case affecting the soles following enteric fever.

There are at least 4 cases in which *injury* may have played a part in the production of the symptoms. The first was recorded by Lewin, and was that of a man who was shot in the right elbow and got ankylosis of the elbow-joint; some months afterwards erythromelalgia appeared in his right index, ring, and little fingers. Another case is recorded fully by Weir Mitchell in his last memoir; the symptoms followed upon the fall of a heavy piece of stone on the patient's foot in front of the right ankle; the wound was superficial, but there was considerable swelling of the foot and leg. Six weeks later a swelling on the sole was incised, but there was no evidence of suppuration and only slight bleeding. Signs of erythromelalgia gradually appeared with the addition of fine rhythmical tremor affecting the whole leg, an increased knee-jerk, and ankle-clonus. Weir Mitchell was of opinion that neuritis of the foot was set up by the injury. At his suggestion portions of the internal saphenous and musculo-cutaneous nerves were resected, and the two plantar nerves were stretched. Some anaesthesia was induced; marked relief of the pain followed, and gradual subsidence of the flushing. In two months' time the patient could walk; and six months later he was at his work and free from pain. Microscopically, however, the resected nerves were normal. In Dr. J. R. Bradford's (57) case a blow on the back of the hand led to the formation of an abscess which slowly healed. Some years elapsed before severe erythromelalgia supervened, but it undoubtedly extended from the scar as a centre. In a case under my care (p. 154) chronic swelling caused by a severe blow on the back of the hand was the immediate starting-point of intractable erythromelalgia.

Morgan attributed one of his cases of limited erythromelalgia of the hand to long-continued hammering. Exposure to fatigue, as in long marches, seems to have played an important part in the causation of several cases. Whatever the primary cause, a long walk has sometimes precipitated a relapse.

Dreschfeld and Morgan's case, of a collier who worked for hours in a mine with his feet in cold water, has already been mentioned; and this may be paralleled by Sir J. Paget's case of a man who endeavoured to harden himself every morning by cold shower-baths, and by standing in cold water up to the knees. After eight days of such experiments the limbs became cold, benumbed, and marble-like.

One of the most interesting coexistences is recorded by Dr. E. S. Reynolds. In the Manchester series of arsenical beer poisoning patches of erythromelalgia occurred, especially in the palms and soles.

**Pathology.**—Since this group of symptoms, striking as it is, has so many different antecedents, and exists in so many different combinations, it may well be asked, is the pathology always the same? In other words, is one constant mechanism always present, whatever the superadded conditions may be? To this question no answer can be given; chiefly because the results of anatomical and microscopical investigation are so meagre. There are at least four directions in which inquiry should extend: namely, to alterations (*a*) in blood-states, (*b*) in peripheral nerves, (*c*) in brain and cord, especially as to the vasomotor centres, and (*d*), lastly, in the blood-vessels.

(*a*) Of the direct bearing of altered blood-states the evidence is very meagre. There may be sometimes a link with albuminuria and glycosuria, but it is not, so far as we know, a close or a frequent one. When it occurs it is probably by way of a vascular alteration to be subsequently considered. There is no adequate justification to connect erythromelalgia immediately or directly with gout or rheumatism. The coexistence of occasional pain referred to joints or muscles is not surprising, considering the frequency of such pains in people of all classes in our climate. The noxae associated with faulty digestion, which often give rise to temporary acroparaesthesia in its various forms, such as numbness and tingling in the extremities, have apparently little if any relation to cases of erythromelalgia. Beyond its occurrence in rather slight recoverable form on the palms and soles in arsenical beer poisoning described by Dr. E. S. Reynolds, we have little evidence as regards toxic causes. Investigation is much needed as regards the influence of plumbism, alcohol, and tobacco. The comparative infrequency of the association with any of the acute infectious diseases or malaria or septicaemia, either as a complication or a sequel, is remarkable. It is difficult to prove that syphilis plays any direct or immediate part in its etiology, though it may have a decided remote share in inducing vascular changes. Thus, to sum up, our limited knowledge of altered blood-states gives us very little help as to their bearing on the causation of erythromelalgia.

(*b*) The occasional combination of erythromelalgia with different forms of cerebrospinal degeneration does not help to explain the disease, for erythromelalgia may exist in its most intense form without any indication whatever of central nervous disease.

(*c*) and (*d*) Weir Mitchell (40) attaches great importance to Auerbach's case, which presented some degeneration of the posterior roots of the lower lumbar and upper sacral nerves, although the peripheral nerves were normal. But the case is singularly inconclusive, for Auerbach admits that degeneration of the posterior roots often occurs without erythromelalgia, and certainly erythromelalgia exists without any evidence of disease of the posterior roots. According to Sachs there was clinically some suggestion of early tabes in Auerbach's patient, so that

the changes in the posterior roots may have been related to that disease, rather than to the associated erythromelalgia. The most striking point about the uncomplicated cases of erythromelalgia is, that they begin locally; and there is a certain amount of evidence that protracted local exposure to varying temperatures, local fatigue, and local trauma are important antecedents. Many cases begin locally and remain local for years, and in other cases the subsequent spread is quite as compatible with fresh local foci of disease as with a central origin. Do the phenomena of erythromelalgia depend on primary peripheral neuritis? The clinical reply is that no definite localised anaesthesia can be made out during the semi-quiescent periods, that with the rarest exceptions localised atrophies of muscles cannot be detected, and that there is no reaction of degeneration. The widespread lowered nutrition of the tissues and the degree of generalised muscular atrophy sometimes present would explain, especially in the chronic cases, some atrophy of nerve-fibres, but would not account for typical primary inflammatory changes of separate nerve-trunks.

The marked alternations of vascular tone with the attendant colour-changes, localised heat, and occasionally hyperidrosis, have suggested that, just as a neuritis may be chiefly sensory or be both motor and sensory, in this disease there is a neuritis confined to, or mainly affecting, the vasomotor fibres. The main objection to such a hypothesis is the absence of any anatomical or even experimental proof that the vasomotor paths in the nerves have separate conducting fibres. In 1903 Dr. Batty Shaw analysed the 9 reported cases of erythromelalgia in which the condition of the peripheral nerves had been investigated. The last case recorded by Weir Mitchell and Spiller was a man aged sixty-one, whose big toe with part of its metatarsal bone was amputated. Examination shewed some reduction of the number of nerve-fibres in a portion of excised nerve, some degenerated fibres, and some increase of fibrous tissue. It is important to add that in some of the arteries the lumen was nearly closed by proliferated intima and thickened media. In Auerbach's case, already mentioned, the peripheral nerves were normal, but the vessels apparently were not examined. In Weir Mitchell's first case the nerves were normal, and the small arteries were thickened; in his second case the portions of nerve which were removed were found free from disease. In Dehio's very important case, of erythromelalgia of the hand and foot, a portion of the ulnar nerve and an equal length of the ulnar artery were removed. The nerve was normal, but the artery shewed thickening of both middle and inner coats and some narrowing of the lumen. Sachs's patient was a Russian tailor, aged thirty, with erythromelalgia of the left foot and calf. The case was typical, except that in addition to the generalised atrophy there was marked wasting in the region of the peronei. Gangrene of the toes necessitated amputation through the thigh, which was followed by a good recovery. The changes in the nerves were slight, and were best marked in the peroneal, the sciatic and internal popliteal being very little altered. No



single nerve-bundle was completely degenerated, though individual nerve-fibres were degenerated and in some places shewed fibrous substitution. There was not, however, any cellular infiltration of the nerve-sheaths or perineuritis. On the other hand, the arteries were very extensively diseased; all the coats were affected, but the intimal changes were the most marked. Several branches of the popliteal were quite closed, and the small arteries accompanying the nerves were often completely obliterated. The walls of the veins also were moderately thickened. Sachs maintained that the changes in the nerves were so slight that they could not be held responsible for the arterial disease, and that it was highly probable that the widespread obliterating arteritis was sufficient to explain the atrophy and fibrosis of the nerves. In the 3 cases investigated by Dr. Batty Shaw (of which one was a patient of my own) the nerves were found free from morbid change; there was no degeneration and no increase of fibrous tissue. In all arterial thickening was found, and in some of them thickening and thrombosis of the veins likewise. In an allied case of Dr. Parkes Weber's similar changes were present in the walls of the arterioles of the skin and the muscles, but the nerves were normal. The rarity of these cases makes it important that all the available pathological observations should be recorded; I therefore append a very brief account of 2 cases under my care in which the condition of the vessels and nerves was critically examined:—

*Case 1.*—A hard-worked general servant, aged twenty, damaged her right wrist, which nine months later was incised on several occasions, healing being much delayed. There was no evidence of tuberculosis. The right hand and wrist became extremely painful, swollen, and red, and was a characteristic example of erythromelalgia. By Oliver's arteriometer the right radial artery was shewn to be a third the size of the left. The pain was so severe and so intractable to treatment that amputation through the forearm was carried out: at the operation it was noticed that there was less bleeding than is usual. (I may perhaps mention that in another case of this nature under my observation amputation of foot was performed without any ligatures being necessary for the arteries.) After amputation of the arm the patient made a good recovery; the vessels and nerves were examined by Dr. Batty Shaw (57). Four years later the patient returned with a similar condition of erythromelalgia of the left hand, which was eventually amputated. Dr. G. Hall found that the radial, ulnar, and digital arteries shewed considerable fibrotic thickening of the media; the intima was irregularly affected, but not sufficiently so to obliterate the lumen. There was no evidence that the vessels and nerves were embedded in, or compressed by, fibrous tissue. The companion veins of the larger arteries were fairly healthy. The small arteries of the skin shewed thickening of the media, but the most marked change in the skin was in the small veins which presented much irregularity and thickening with large projections into the lumen, which was often divided as the result of thrombosis and subsequent canalisation. The nerves were healthy, and their smaller branches were clearly made out.

*Case 2.*—A housewife, aged forty-four years, had had pain for two years, slight



in the right, severe in the left foot. The pain was increased by attempts to walk or when the legs were allowed to hang down. These symptoms came on after a severe flooding. She had had six healthy children and five miscarriages. On admission, she complained of coldness, swelling, and pain in the left foot. Her fingers were thin, cold, and a little blue. Pulsation could be felt in the popliteal and posterior tibial arteries, but not in the dorsalis pedis on the left side. The right foot was cold, but not blue or painful; slight pulsation could be felt in the dorsalis pedis artery on that side. For a time the application of Bier's bandages was thought to be beneficial, but the effect was transient, and after eighteen weeks amputation was successfully performed. Dr. G. Hall found that the larger arteries shewed little change in the media and slight irregular proliferation in the intima; the companion veins were relatively more affected, the intima being markedly thickened in an irregular manner. The smaller arteries of the foot, both deep and superficial, shewed thickening of the media and a more advanced change in the intima than was seen in the larger vessels. Many of the smaller veins of the skin were almost occluded by intimal thickening and thrombosis, some being quite occluded. There was not any gross matting of the perivascular tissues, but the adventitia was moderately thickened in some of the arteries, and there was some evidence of affection of the vasa vasorum. The nerves were quite normal.

If there is a fair presumption in favour of the view that obliterating arteritis, especially of the smaller arteries, is a true factor in the production of erythromelalgia, and if a certain degree of atrophy of some of the nerve-fibres may be regarded as the result of the arterial disease, we may inquire whether any forms of disease known to depend on arterial obstruction adequately resemble erythromelalgia. Chareot described a group of cases as manifesting what he called *intermittent claudication*. These are cases mostly of men in early middle life who suffer from intermittent attacks of paresis, usually of one leg, associated with severe pain, paræsthesia, some stiffness, and a varying amount of vasomotor disturbance. The characteristic feature is that these intermittent attacks of weakness and pain are brought on by walking, and that in the early stages of the disease the symptoms disappear with rest, and recur when the walking is resumed. Very similar attacks in horses have long been known (4). Charcot's pupils published a considerable number of examples in men and some in women, but the most instructive series has been given by Erb under the title of *intermittent limp*. In some of these cases the vasomotor disturbance is closely allied to erythromelalgia, and the way in which the symptoms are precipitated by muscular effort and dissipated by rest in the horizontal position is singularly parallel to the alteration with the dependent position in Weir Mitchell's disease. Many of these cases become chronic, and then the pain is more or less continuous and in not a few cases gangrene of varying extent has supervened, and amputation has been performed and opportunity has been afforded for anatomical investigation. In most of the cases there has been more or less obliteration or narrowing of one or more of the arteries to the feet. Chareot and his pupils attached the greatest

importance to interference by aneurysm in the pelvis or by other causes leading to obstruction of one of the larger arterial trunks high up, in consequence of which, though collateral anastomosis had been moderately established and the general circulation and nutrition of the limb had been so far restored or maintained as to be adequate during the state of quiescence, yet it was not adequate when by muscular effort a greater afflux of arterial blood, especially to the muscles themselves, was required. Charcot pointed out that this demand, which could not be adequately supplied, gave rise to a condition of temporary arterial spasm, to which he gave the name of claudication.

But in his later papers Charcot recognised that arterial sclerosis of the more distal portions of the arteries of the limbs could also cause intermittent claudication. He instanced similar phenomena of arterial ischaemia in other vascular regions, for example angina pectoris due to spasm and contraction of the coronary arteries, and also to what he called arteriosclerotic giddiness due to spasm of the cerebral arteries. He maintained that the gangrene of diabetes was in part dependent on arteriosclerosis, and referred to intermittent claudication in diabetes as a forerunner of gangrene. Charcot also insisted on the syphilitic antecedents of some of his cases. It is only fair to remember that intermittent claudication, though not under that name, was accurately described by Sir Benjamin Brodie in connexion with obliterative disease of the arteries of the limbs, and Brodie also pointed out the essential similarity of what has been called *angina cruris*, another name for intermittent lameness, to angina pectoris, thus agreeing with the view previously put forward in 1809 by Allan Burns (*vide* Vol. VI. p. 611). In Erb's very thorough and exhaustive records the incidence of obliterative endarteritis on the smaller arteries and arterioles as distinguished from the large trunks was well brought out, and also the occurrence of such local changes in one or other extremity without any necessarily widespread arteriosclerosis. Erb makes the fruitful suggestion that possibly the special incidence of such obliterative arteritis in the arteries supplying the muscles, nerves, and skin may have a bearing on the vasomotor symptoms sometimes coexisting with the intermittent lameness.

Finally, reference should be made to Buerger's anatomical investigation of a series of cases (6), chiefly poor Polish or Russian Jews between the ages of twenty and thirty-five or forty years, in which spontaneous gangrene of one or other of the lower extremities occurred. Here again there was the association of intermittent claudication with erythromelalgia and with the loss of pulsation in the arteries of the feet. Examination shewed obliteration of arteries and veins and a varying amount of periarteritis, hyperplasia of connective tissue, and arteriosclerosis. Such nerve lesions as he found, Buerger held to be secondary, and apparently dependent upon the fibrotic perivascular changes. When the periarteritis was minimal no change in the nerves could be demonstrated, in others some of the nerves were imbedded in a dense mass of connective tissue. Buerger maintained that the endarterial changes were chiefly the result

of thrombosis, and he prefers to designate the condition as an obliterating thrombo-angitis rather than as an endarteritis obliterans. This part of his contention may be deferred for further consideration, but the important point to be noted here is the frequent coexistence and overlapping of erythromelalgia and of intermittent limp in young adults affected with this obliterative disease of vessels.

I suggest that, when a case of erythromelalgia presents itself in which the pulsation of the chief foot arteries is quite up to the normal, there is a strong presumption that the vascular disease may be at an early stage and that its chief incidence may be on some of the smaller vessels, and that at this stage the vasomotor symptoms may be readily produced. When one of the larger arteries of the foot becomes affected, and the obliteration of its lumen proceeds apace, then gangrene may become imminent. But the solid conclusion may, I think, be accepted, that obliterative disease of arteries in the early stage is apt to be accompanied by varying degrees of spasm and succeeding dilatation in collateral arteries, and that alternating states of coldness and hyperaemia, pallor, blueness, and redness may be thereby explained. How much of the pain is dependent on spasm of arteries themselves or altered vascularity of nerves, and even on muscular cramp, we are not in a position to estimate. I submit that such atrophy and fibrosis of some of the nerve-fibres, as is occasionally proved to exist, is probably secondary to the imperfect blood-supply or due to associated connective-tissue overgrowth rather than to primary inflammatory change in the nerves. If the doctrine of the vascular origin of erythromelalgia be the right one, it would not, I think, be difficult to understand that in the cases following local injury in which extensive extravasation has occurred, permanent damage to the sheaths of some of the smaller arteries and veins may have been initiated. This is, I believe, more harmonious with the subsequent progress than the hypothesis of injury to a nerve-trunk.

**Symptoms.**—*Typical Case.*—A man of early middle age, who is engaged in heavy physical work, standing through a long day with exposure to varying temperatures, has had some illness, and returned to his work with lessened vigour. He begins to suffer in the evening with a burning pain in some part of the sole of one foot. The pain is made worse by the standing posture and by walking; it is relieved by lying down, or by raising the leg to the horizontal position. If he is able to rest entirely in bed for some days, not only may the pain vanish during the rest, but he may get relief for a time; if, as is more commonly the case, he goes on with his work, the pain, though temporarily relieved by rest, returns a little earlier each day, and lasts for a longer time. At this date physical examination gives no clue to the cause of the pain, and an attack of this kind may subside entirely. In the course of a few weeks the pain, after a walk or some other prolonged exertion, may recur with renewed violence; then there supervenes the second characteristic symptom, namely, redness of the foot. At first this is circumscribed; it may affect the heel, the ball of the great toe, one or



other toes, the outer or inner side of the foot. Sometimes there are several small patches. The redness increases in depth and area as the vertical position is maintained, the veins become distended, and the arterial pulsations become excessive. After a time the vascular storm, as it is called by Weir Mitchell, partly subsides; the throbbing ceases, but the foot remains for a time of a purplish-red colour. During the red phase the pain markedly increases in severity, and there may be excessive tenderness to the slightest touch over the red area. Sensibility to heat and cold is increased in the affected foot. Both superficial and deep pressure are resented, but sensation seems otherwise unaltered. The plantar reflex is either normal or exaggerated. During the attack there is unquestionably a local elevation of temperature, which is obvious to the hand of the observer; a surface thermometer may indeed shew that the temperature of the affected foot does not rise as high as the mouth temperature, but it is sometimes two or three degrees above that of the unaffected foot, and it rises during the dependent posture; whereas in the normal state of health, as shewn by Weir Mitchell, the surface temperature of the foot is a little lower in the dependent than in the horizontal position. There is a certain amount of swelling; occasionally the part pits on pressure, but more commonly this is not so: in many cases, however, the swelling has been such as to lead to the suspicion of a true inflammatory affection of the deeper structures or tissues of the periosteum, especially of the os calcis; and fruitless incisions have in some instances been made, even down to the bone.

As with the pain in the early stage, so with the redness and swelling, the vertical position and voluntary movement aggravate, whilst the horizontal position and rest relieve them. It is also found that cold days, cold applications, and free exposure to air bring a certain amount of comfort; whilst hot weather or hot compresses and any degree of pressure increase the severity of the symptoms. Thus, the sufferer refuses to walk; or, if he walks, he treads on the part of the foot which is unaffected; indeed, when the attack is very severe, he goes on his hands and knees. He prefers a bare slipper or even a bare foot to a boot and stocking; and when he lies down he likes to have the weight of the bed-clothes removed by a cradle, or to have his foot exposed to the air, and to bathe it with cold water. There are all degrees of severity. The mild cases may be cured by horizontal rest. Many cases relapse, and generally with increasing severity. The individual attacks, when the disease is established, may last for several hours, even in spite of recumbency; during the intermissions the foot tends sometimes to become nuduly pale. The disease may last for many years; in one of Morgan's cases it continued for twenty-seven years, limited to one sole. Generally after long periods the exacerbations of the pain tend to diminish, as also do the changes of colour on alteration of position.

Taking the above case as one in accord with the type, there are many variations to be considered. The burning pain, though not so striking as the vasomotor phenomena, is really the most important symptom, because



almost invariably it is the initial one. It is important, however, to note that, in Sigerson's case, which was a multiple one, there were vasomotor phenomena corresponding to those of the type, but in the history no record of pain. Also some of the other multiple cases, which shewed in certain extremities the triple symptoms—pain, redness, and swelling—nevertheless presented severe pains elsewhere also, which were unaccompanied by vasomotor signs: namely, pains in the back of the head and neck, both before (Benda (35)) and subsequent to the erythromelalgia (Gerhardt); pains in one shoulder and elbow, along with and succeeding erythromelalgia in the feet (Strauss); slight burning in the feet, with erythromelalgia in the hands (Weir Mitchell's case v.). In Sir J. Paget's case, which is probably one of the connecting links with Raynaud's disease, the pain appeared in the feet with extreme pallor (local syncope), which preceded the redness and swelling. During the red swollen stage the pain abated.

The characteristic pain is increased more by deep than by superficial pressure. In some of the cases pressure on the distant nerve-trunk, or on the adjacent branch, increased the burning; for example, on the sciatic in a case of Weir Mitchell's and on the internal plantar in a case of Morgan's. But in many cases the adjacent nerves, when they could be reached by local pressure, were not tender; and in other cases, when palpable nerves generally were found to be tender on pressure, this was not more marked in those which could be felt in the neighbourhood of the red areas than elsewhere.

*Distribution of Erythromelalgia.*—Whether it be the foot or the hand, the disease at the outset most commonly attacks one extremity only; and in the simple cases is limited to that extremity. Thus it is primarily asymmetrical. There are several cases recorded of hand affection, though it is not so common nor generally so severe as in the foot. When one or both hands suffer, it is a characteristic attitude for the patient to keep them either crossed over the breast or raised above the head; thus bringing about the greatest possible physiological emptying of the vessels. The disease may attack portions of the other extremities at successive shorter or longer intervals. Further study has shewn a still wider distribution. Thus in Woodnut's case, after successive invasion of some of the toes, first of one foot then of the other, areas of erythromelalgia appeared on the lower part of one leg and over the middle of the back. In Benda's case there were rose-red areas on both sides between the mastoid regions and the neck, which were hot and painful, both spontaneously and on pressure, and accompanied by distinct erythromelalgia of the outer side of the right foot. In the case recorded by Anché and Lespinasse, along with erythromelalgic attacks in one upper and one lower extremity, there was much congestion of the face, eyes, and external ears; and one testicle became swollen and tender. Finally, Seeligmüller's case shews a still more remarkable distribution: a woman, aged fifty-six, had for two years burning pains in the left hand and right foot; then came redness and swelling of the finger-ends as well as of the toes and ball of the foot. At the beginning of the periodical attacks she

had the feeling as of a hot ray from the shoulder down to the fingers; and the head, neck, and mucous membrane of the mouth, throat, and gums became markedly hyperaemic.

*Skin.*—Weir Mitchell lays great stress on the colour in erythromelalgia, as distinguished from the blue-black colour of the local asphyxia of Raynaud; it is a rosy-red at first, and ultimately, in the later stage of the vascular storm, purplish-red. But in several of the chronic cases, in which the painful phases had lessened in severity, it is expressly recorded that the extremities became cold and either pale or livid.

With respect to other skin changes; vesication is sometimes found in the acute stage, and small nodules may appear in the red areas. Hardening of the cellular tissue, tense and shiny finger-ends, or actual clubbing and thickening of the nails, occasionally result. Oedema has been recorded, in some of the chronic cases, as a late condition. The occasional simulation of a deep inflammatory effusion in erythromelalgia, especially in the sole, has been already mentioned. The surface temperature of the feet in the chronic cases is generally notably lower than that of the mouth.

The muscles of the affected limbs usually shew slight general wasting. It is doubtful whether this is more than is to be explained by the pain and enforced disuse of the limb. It is certainly insignificant in amount as compared with that commonly seen in well-marked peripheral neuritis; and, as a rule, muscles are not picked out individually. The only important instance of extensive wasting was Eulenburg's case; an anaemic woman, after her second attack of erythromelalgia, presented muscular dystrophy, of Erb's juvenile type, affecting the upper arm and shoulder of both sides. In no case are degenerative reactions to the constant current recorded. In Allen Sturge's case there was slight diminution of electric irritability; and in one of Weir Mitchell's cases slight quantitative increase to both currents, but no qualitative change. Only in one case (44) is the knee-jerk recorded as absent. In 2 of Weir Mitchell's cases it was increased.

We have now to enumerate briefly some of the various symptoms which have been found in the subjects of erythromelalgia, concerning which, in our present knowledge, it is impossible to say exactly how far the relation was an essential, and how far an accidental one; these relate almost entirely to the nervous system.

There are several examples of psychological changes, some of which are probably hysterical, or at all events temporary; others, however, are persistent or progressive, and associated with definite paralytic signs, such as hemiplegia, speech-defects, or spinal cord degeneration. Thus Weir Mitchell's second patient, a man aged thirty-five, about six years after the onset of his erythromelalgia, became very morose, and would only answer questions in whispered monosyllables. He had some seizures, in which he became rigid and was drowsy. He complained of girdle-pain, and shewed for a time a fine tremor on muscular effort, ankle-drop, and weakness of grasp. He ultimately presented excessive reflexes,

spastic knee-jerks, and ankle-clonus. Weir Mitchell's judgment was, that during the twenty-three years that this patient suffered, hysteria and some spinal cord lesion supervened on the erythromelalgia which, indeed, latterly diminished markedly. A woman, aged forty-four, who was under the care both of Gerhardt and Enlenburg, had well-marked erythromelalgia in all four extremities. In one of her attacks she got pains in the tongue, and some difficulties of speech. By degrees the painful element in her limb attacks diminished, and the extremities became cold and livid; but signs of central disturbance appeared. Besides suffering from pains in the head and neck, and giddiness, she became uncertain in her gait. Gradual failure of intelligence and memory with hallucinations supervened, and changes in the fundus oculi were discovered. A woman, aged fifty-seven years, was the subject of erythromelalgia of the back of the neck, shoulders, and one foot. On this there supervened some weakness of memory. The speech was slow and difficult; the pupils were immobile and the knee-jerks exaggerated (Benda). Although in this case syphilis was denied, it was a possible factor, as double sixth nerve paralysis had preceded the erythromelalgia, and there was a history of three stillborn children. There was also partial improvement after the use of iodide of potassium, and of baths and faradism.

In several cases vertigo and pain in the head were induced by assuming the erect posture. A medical student, aged twenty-one, whose case is described by Lewin and Benda, was the subject of severe migraine with hemianopsia, and without any obvious cause got erythromelalgia of the left hand. While suffering from this affection, a temporary paralysis of the left arm and leg followed upon three days' vomiting and giddiness. But the erythromelalgia remained unchanged, and he suffered pains in the right hand, though without redness or swelling. In Graves' case, a woman of eighty-two, there was a slight attack of left hemiplegia with headache, vertigo, and sight troubles. This was followed, in one month, by erythromelalgia of the right foot, which, after considerable suffering, subsided in about three months. In another month she suffered a second stroke and died. Hensch records the case of a man, who, while undergoing a bath cure, was seized with paresis and anaesthesia of the left half of the body. From this after a few weeks he recovered, but a liability to frequent sweating on the left side persisted. Six months later erythromelalgia of the left foot appeared; after this came angina pectoris, and albuminuria with signs of arteriosclerosis, and finally he died of cerebral haemorrhage. In Machol's case erythromelalgia appeared in the last stage of a case of paralytic dementia; and there are 2 cases (Landgraf's and F. P. Henry's) in which it appeared in patients with myxoedema.

There is at least 1 case (Edinger) in which erythromelalgia occurred in the course of tabes; and another (Woodnut) in which lightning pains in the arms and legs, and some lessening of sensation in one lower limb, apart altogether from the red areas, were suggestive of early tabes.



Dr. J. Collier reported 6 cases of disseminated sclerosis, 2 cases of tabes, and 1 of chronic myelitis in which erythromelalgia occurred. Pospelow has recorded a case of syringomyelia in which erythromelalgia supervened in one hand and one foot.

**The Relation between Erythromelalgia and Raynaud's Disease.**—The differences have been tabulated by Weir Mitchell, and the following enumeration embodies his table, with some important modifications arising out of recent pathological observations :—

1. They are both affections of the extremities of the body. Local asphyxia is generally symmetrical, similar extremities being primarily attacked in the majority of cases, though possibly in unequal degree. Erythromelalgia, on the other hand, is at the outset, and for a considerable time, definitely one-sided, and it may remain so to the end.

2. Local asphyxia is paroxysmal at first and generally so throughout. During the intervals there is restoration to the normal state. Erythromelalgia, though liable to exacerbations and in its early stages to remissions, and in certain cases to spontaneous subsidence, may persist with little change in the symptoms for years, or may go steadily and slowly from bad to worse.

3. The immediate determining condition of local asphyxia is, in most cases, exposure to cold; and local asphyxia is pre-eminently a cold-weather disease. The immediate determining conditions of erythromelalgia are dependency and muscular movements of the extremity concerned. There is no special seasonal incidence.

4. Raynaud's disease is much more common in females than in males, and thus agrees with the greater incidence of vasomotor disturbances generally in females than in males. On the other hand, there is a preponderance in the incidence of erythromelalgia in males over females; this is in harmony with the greater liability of men than of women to organic disease of the blood-vessels.

5. Raynaud's disease occurs at all ages, and there are many examples amongst children; it would appear often to be a congenital vice of the circulation. The commonest periods for erythromelalgia are early and middle adult life.

6. The characteristic colour-changes of Raynaud's disease are pallor and blueness associated with coldness of the extremities concerned, the return to the normal state being ushered in by a reaction stage, during which the extremities become red and hot. The early characteristic colour-change of erythromelalgia is a dull pink or salmon colour associated with a feeling of burning experienced by the patient, and some local elevation of temperature appreciated by the observer. This is brought on by dependency and muscular effort, and gradually subsides when the limb is brought back to rest in the horizontal position. In the later stages of the disease it is important to emphasise that this pink colour becomes less marked. Indeed, it often disappears and is replaced by pallor and slight blueness.

7. Both diseases are sometimes accompanied by more or less general-



ised vasomotor disturbance. This is more marked in Raynaud's disease than in erythromelalgia, and it occurs earlier in the course of Raynaud's disease than in erythromelalgia.

8. The permanent alteration in the shape of the extremity, which sometimes occurs in Raynaud's disease, is in the direction of atrophy with occasional slight contraction. Any tumefaction that occurs in Raynaud's disease is temporary. In erythromelalgia permanent tumefaction is common.

9. Gangrene may occur in both these disorders. In local asphyxia it is more commonly symmetrical and superficial. In erythromelalgia it is local and deeper in its invasion.

10. The distinction which I suggest underlies the clinical differences is that Raynaud's disease is primarily a symmetrical vasomotor affection, although, ultimately, permanent disease of the vessel-walls may supervene: whilst in erythromelalgia there is primary localised disease in arterioles and venules of the skin, subcutaneous tissues, and muscles, with varying accompanying vasomotor disturbance of the collateral vessels.

**Prognosis and Treatment.**—In view of the provisional explanation that I have given of the mechanism of erythromelalgia, it is not surprising that its prognosis is most unfavourable. As regards treatment, it may fairly be placed amongst the *bêtes noires* of medicine and surgery. In the very early stage the disease is often difficult to diagnose, for in most cases the pain antedates the colour-changes. Given the cardinal symptoms—inexplicable pain following on the dependent position, increasing with walking, entirely disappearing with return to horizontality—it would seem that the right practice is to send the patient to bed and keep him there for some weeks, and to endeavour to improve his general nutrition, and to secure, as far as possible, adequate elimination of morbid products. If there are any colour-changes or local heat, or if the pulsation of one or other foot artery be difficult to identify, these signs should emphasise our decision; and we should be just as insistent about horizontal rest, or even raising the limb, as in a case of threatened gangrene or of acute phlebitis. Certainly, if there were the least suspicion of past syphilis, iodides should be given, and even in the absence of all evidence it would probably be right to give iodides a trial. Some of Friedländer's cases of obliterative endarteritis improved under the administration of iodides even in the absence of any evidence of syphilis (*vide* Pearce Gould's case).

Erb lays great stress on alcoholism and excessive smoking as factors in some of his cases of intermittent limp. I am not able to give any personal experience on these points, but nicotine is a powerful vaso-constrictor, and symptoms indistinguishable from angina pectoris have been induced by over-smoking (*vide* Vol. II. Part I. p. 984). Alcohol sometimes mitigates the pain of erythromelalgia, and, when given for that purpose, has sometimes led to incurable alcoholic excess. When in doubt in these cases, it is, I think, advisable to forbid both alcohol and tobacco altogether.

The bare possibility of some local or remote cause of perivascular obstruction should always be kept in mind, especially in the markedly unilateral cases. This is illustrated by the following case:—

A lady, aged thirty-nine, had suffered within the last eighteen months with erythromelalgia of the left foot; ultimately, pulsation in the femoral and in some of its branches disappeared, and gangrene supervened in the left big toe, which had to be amputated. During this period she was attacked with appendicitis, though it was almost certain that she had suffered from previous slight attacks of it. There was much suppuration found around the appendix, which was gangrenous. The appendectomy was apparently successful, but much inflammatory thickening was left in the pelvis. When I saw her, nine months after the initial operation, erythromelalgia still appeared whenever she walked, and was relieved when she kept her bed. The occlusion of the femoral artery and of its main branches was very obvious; there was considerable matting of tissues in the pelvis and a massive swelling in the left iliac fossa, probably due to chronic inflammatory material which firmly fixed the uterus. There was occasional slight pyrexia. On Dr. Beauchamp's urgent recommendation, Sir Watson Cheyne reopened the old appendectomy wound and found a small abscess in the stump of the appendix, and most extensive adhesions filling the pelvis and fixing the uterus and the annexa. He freed many of these adhesions, and evacuated the small abscess. The result on the erythromelalgia, as well as on the general health, was very remarkable, although the patency of the occluded femoral artery was not completely re-established. Four months afterwards a very distinct, though faint, pulsation was felt in it, and there was undoubted improvement in the circulation and the general nutrition of the left lower limb. The patient became free from spontaneous pain, and could walk quietly for some distance without bringing it on, though if she tried to run, a little of the old pain reappeared in the foot. The galvanic bath treatment was continued for a considerable time after recovery from the second operation, and probably with benefit; but I am convinced that the removal of the constricting adhesions around the vascular supply of the lower limb was a most important factor in facilitating a more efficient collateral circulation, and so relieving the erythromelalgia. This case recalls one of Charcot's early examples of intermittent claudication, in which an iliac aneurysm caused obstruction of the femoral artery and its branches.

With respect to local deep-seated damage in some of the cases of erythromelalgia following upon injury, it is true that incisions, which have in some cases repeatedly been made, have not been followed by permanent benefit as in my first case (p. 154), though they may have given temporary amelioration. But, so far as I know, no surgical attempt in any of the traumatic cases has been made to ascertain whether the vascular trunks are embarrassed by surrounding connective-tissue growth, and, if so, to free them. It has been suggested that in some of these cases, as in threatening arteriosclerotic gangrene, the operation of arterio-

venous anastomosis might be attempted. Buerger (7) has pointed out some of the difficulties arising from our ignorance as to the patency, or otherwise, of the deeper veins, but careful exploration would at least reveal some of the possibilities of dealing with the condition, and, as above suggested, of relieving any perivascular thickening that might be present.

Besides rest in the horizontal position, the value of which is undoubted, the local application of cold sometimes relieves the pain to a slight extent, whilst hot applications make it worse. Galvanism may help the general nutrition a little, but it does not influence the pain. In the few experiences that I have had with Bier's bandages, no permanent improvement has ensued.

Weir Mitchell records two cases in which removal of small portions of nerves and stretching of other nerves was practised (41). In one case benefit ensued, and, microscopically, the portions of nerve were found to be healthy. In his second case gangrene followed the operation, and the patient died during a subsequent amputation. Limited amputation, for example, of a gangrenous toe, has been moderately satisfactory as regards recovery of the operation, but is not by any means necessarily successful as regards complete release from pain. Amputation of either an upper or a lower limb for severe and protracted erythromelalgia, in which gangrene has not yet supervened might, at first sight, seem an extreme and unjustifiable measure. Every case must be judged on its merits. Intractable as most cases are, we must always remember the occasional spontaneous subsidence of symptoms after long periods of suffering, especially when prolonged recumbency has been maintained. But anybody who has witnessed, in a severe case, the advancing exhaustion and continuous, almost unrelievable distress, even under repeated doses of morphine, will not have the courage to refuse this last chance, which in 2 of my cases (*vide* p. 154) was certainly amply justified.

THOMAS BARLOW.

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T. B.

## FACIAL HEMIATROPHY AND HEMIHYPERTROPHY

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**FACIAL HEMIATROPHY.** *Synonyms:* *Hemiatrophia facialis progressiva*; *Umschriebene Gesichtschwund*; *Hémiatrophie faciale*. **Introduction.**—This is a relatively rare disease. The characteristic changes begin more commonly before puberty than after it; no true instance of this condition occurring after thirty years of age is on record. The disease is commoner in women than in men.

In a few cases a direct heredity has been traced, whilst various exciting causes have been assigned. In some cases it is probable that acute infectious disease, such as scarlet fever, measles, enteric fever or erysipelas, and such morbid conditions as tonsillitis, influenza, and abscess in the neighbourhood of the ear may have been the direct excitant; and in others some injury has been noted shortly before the onset of the disease.

It may be fairly stated that in the majority of cases no obvious cause is to be found.

**Pathology.**—There are 5 cases on record in which a necropsy has been made, but in only one of these (case of Virchow and Mendel) has the pathological condition been fully described. This was a pure case of old-standing facial hemiatrophy. The trigeminal nerve shewed microscopically the pathological appearances of a proliferating interstitial neuritis; the facial nerve was normal. The principal changes discovered in the central nervous axis were atrophy of the so-called descending trigeminal root and of the cells of the *substantia ferruginea pontis*.

Mendel's contention is that the facial hemiatrophy is brought about by the interstitial neuritis, and that the atrophy of the descending trigeminal root supports Merkel's view that this is the "trophic" root of the fifth nerve. But it is doubtful how far the cutaneous condition is directly due to the nerve lesion. It will be shewn elsewhere (*Art. "Cranial Nerves,"* p. 519) that the so-called "trophic" root of Merkel does not contain trophic but motor fibres. A careful study of Mendel's paper shews that, notwithstanding the existence of the interstitial neuritis, most of the trigeminal nerve-fibres were normal; it appears, therefore, more logical to regard the nervous and cutaneous lesions as arising from one and the same cause, and not as cause and effect.

The older views upon the causation of facial hemiatrophy may be

now disregarded, for they are based, not upon actual pathological facts, but upon speculative considerations. Hence it is scarcely necessary to do more than refer to the "trophoneurosis" of Romberg; the "vasomotor" surmise of Stilling; and the doctrine of "sympathetic affection" propounded by Seeligmüller and others. The view most in harmony with all the facts seems to point to an arrest of development during, or towards the end of, the growing period. What the cause of this arrest may be is doubtful; according to Sir J. Hutchinson, it arises from a morphoea of the fifth cranial nerve.

**Symptoms.**—The first symptom is usually the appearance upon the cheek, chin, or forehead of a white, or whitish-yellow, spot or patch. Originally somewhat ill-defined and limited in size, this patch gradually increases, in some instances by the agglomeration of other similar spots. The skin over this area assumes a parchment-like appearance, in many cases being distinctly "glossy"; and, if the disease begin on the cheek, a well-marked depression under the malar bone, due to atrophy of the subcutaneous fat, readily attracts attention. The rapidity and extent of the change vary in different cases; in some, the affection is limited to one part of the face, the commonest site being the cheek and adjoining parts; in this case one side presents a curious shrunken appearance, the atrophy being limited by the middle line.

In addition to the alterations in the true skin the subcutaneous fat is largely affected, so that in the centre of the patch this tissue is conspicuously absent.

Should the change involve the eyebrows, or hairy parts of the face, these are observed to change colour; and in some cases the hair thins and falls out. Sweating and other cutaneous secretions are sometimes lessened on the atrophied side.

Microscopically the epidermis has not been found definitely affected, but the skin papillae are atrophied, and there is a general thinning of the connective tissues, and atrophy of the subcutaneous fat.

These are the earlier and characteristic changes of facial hemiatrophy—the disease beginning in the skin and subcutaneous fatty tissue. The shrinking in size of the bones and muscles, to be mentioned presently, are later changes. Möbius has pointed out that in the cases in which a lesion of the cervical sympathetic nerve has caused a false appearance of hemiatrophy the skin and fat are not atrophied.

*The facial muscles* in old-standing cases are thinned from atrophy, and absorption of fat; but they do not shew any degenerative change, nor any paralysis of movement volitionally or in emotion, except in so far as the sclerous condition of the skin acts as an impediment. They shew no degenerative electrical reaction. The faradic excitability of the muscles of the atrophied side is often increased; but this arises from the lessened resistance to the current owing to the disappearance of the subcutaneous fat.

An associated hemiatrophy of the tongue has been noted in some cases; but this atrophy is not the muscular change which occurs in true

lingual hemiatrophy from lesion of the hypoglossal nerve or nucleus. The reactions of the lingual muscles are not altered.

*The bones of the face* become shrunken, the change affecting the frontal, malar, and the upper and lower maxillary to an equal extent. The osseous atrophy is greatest in those cases in which the change began before or at puberty, but is not confined to them. The nasal cartilages usually share in the general atrophy; the ear is least affected.

Neither *common sensation* nor the sense of taste is affected.

Various *associated symptoms* have been described,—for example, neuralgic pains over the area of trigeminal distribution, twitching of the facial muscles, and symptoms of affection of the cervical sympathetic nerve.

For purposes of description and classification, the following forms have been described: (a) complete unilateral cases; (b) incomplete unilateral cases. Most instances belong to the latter variety in the early stages, but some have been recorded in which the disease was apparently limited to special parts; for example, Dr. Gulland's case, in which the atrophy was limited to the first division of the trigeminus, and Bärwinkel's case, in which the atrophy was limited to the second division. (c) Bilateral cases. (d) Cases with implication of other parts of the body; for example, the case of Virchow and Mendel, and that of Sir J. Hutchinson.

The **differential diagnosis** is to be made from several other conditions; but there is little difficulty in recognising the true facial hemiatrophy, when it is borne in mind that the essential change lies in atrophy of the cutis vera and subcutaneous connective and fatty tissues. The conditions which bear a superficial resemblance to this disease are: (a) congenital facial atrophy and other asymmetry; (b) facial asymmetry in infantile hemiplegia; (c) facial and trigeminal palsy with muscular atrophy; (d) palsy of the cervical sympathetic nerve.

Little need be said regarding **prognosis**. In the majority of cases the atrophic process is progressive, although in some it has been spontaneously arrested; the disease has no tendency to shorten life. The atrophy in the large majority of cases is confined to the face, commonly to one side of it; and in a few rare instances to a portion of one side.

The **treatment** lies in the administration of general and nervine tonics and in local applications to the skin of the face. Amongst the former may be mentioned quinine, iron, arsenic, and strychnine; the latter consist of gentle massage, carefully regulated facial gymnastics, and the application of electricity, preferably the constant current.

**FACIAL HEMIHYPERTROPHY.**—Scattered throughout medical records are a few rare cases of what may be regarded as the converse of facial hemiatrophy, namely, unilateral facial hypertrophy. Dr. Mackay has collected 29 cases, 17 in females, 12 in males; in 23 cases the condition was congenital, in 6 it was acquired. The change, which consists in an

increased growth of the tissues of the affected region, involves not only the bones but also the soft parts. Thus the skin over the forehead, cheek, and chin is rough, coarse, and thickened—a change which equally affects the hair and sebaceous follicles. The bony enlargements are specially noticed on the forehead, supra-orbital ridge, and malar prominence.

In 2 cases in which the skull was examined after death (Hutchinson, Thomson) the bony overgrowth consisted of a general osseous hypertrophy with the addition of broad-based exostoses, large and small, limited exactly to one side of the skull, face, and jaws. Similar changes were noted on the palate, basilar process, and sphenoid bone. These exostoses were not limited to the external surface, for in places they were also observed projecting into the cranial cavity. The osseous change is of the nature of a true hypertrophy; for, in addition to the points already noted, there were found enlargement of the cancellous structure, distension of the natural sinuses, and of the vascular and nervous canals (Thomson).

Even less can be said of the cause of this hypertrophic condition than has been stated with regard to hemiatrophy. In the recorded cases the change has been limited to the area of distribution of the fifth cranial nerve. But there is as much difficulty in accepting the view that the hypertrophy is due to an exalted "trophic" influence of this nerve, as in believing that the conversely atrophic condition arises from a diminished "trophic" influence. In the atrophic instance the change is one of arrested development; and in the hypertrophic condition it appears to be an evolutionary development of a precocious nature during the growth period.

Dr. Mackay concludes from a careful consideration of the subject that the most reasonable explanation is that which associates it with disturbance of hypothetical nutritional or trophic centres. In some of its features facial hemihypertrophy appears to have a relationship with syringomyelia and acromegaly.

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W. A. T.



# DISEASES OF THE NERVOUS SYSTEM

INTRODUCTION TO NEURO-PATHOLOGY.

TREMOR, "TENDON-PHENOMENON," AND SPASM.

MEDICAL OPHTHALMOLOGY.



## AN INTRODUCTION TO NEURO-PATHOLOGY

By FREDERICK W. MOTT, M.D., F.R.S.

THE NEURON CONCEPT IN RELATION TO NEUROPATHY.—The histological elements which make up the nervous system may be divided into two groups: (i.) the nervous units or neurons; and (ii.) the supporting, protecting, and nutrient tissues. Organic diseases may start in a primary degeneration of the nervous units or neurons, or the neurons may be affected secondarily by diseases primarily in the supporting, protecting, and nutrient tissues. Such are essentially diseases *within* the nervous system, and include diseases of the blood-vessels, lymphatics, membranes, and special nervous connective tissue (neuroglia). These give rise to secondary degeneration, either by direct injury, inflammatory compression, or by cutting off the blood-supply.

The causes of pathological processes occurring in the nervous system may be considered under two headings: (i.) external, and (ii.) internal; but it may be remarked that in all cases except direct injury the two groups are more or less combined. The external causes depend upon the condition of the blood and lymph by which the neurons are nourished, on the excess or deficiency of normal stimulation, or on the existence of abnormal stimulation. The internal causes depend upon a diminution or loss of the inherent vitality and durability of the neurons themselves. In discussing the causes of degeneration of the neuron it will, therefore, be necessary to consider the experimental and clinico-anatomical observations relating to (i.) failure of the blood-supply; (ii.) toxic conditions of the blood; (iii.) the effect of excess or deficiency of stimulation; and (iv.) inherited defects in the nervous system as a whole or in some particular groups or systems of neurons. But before dealing with the causes of nervous diseases it is necessary to discuss the fundamental principle underlying all neuro-pathological questions, namely, the relation of the nerve-cell to the nerve-fibre.

NEURO-PATHOLOGY.—The pathology of the nervous system may be said to have begun in 1850 with A. V. Waller's memorable communication to the Royal Society: "Experiments on the Section of the Glossopharyngeal and Hypoglossal nerves of the Frog, and Observations of the Alterations produced thereby in the Structure of their Primitive Fibres,"

in which he pointed out that Gunther and Schön had ten years before stated that the primitive fibres at the end of a week after division of the nerve, and when it had lost its irritability, shewed changes indicating degeneration; and that Nasse and Steinruck had also described changes following division of nerves. Waller's researches proved that a change took place throughout the whole of the nerve below the point of section and extended to its terminal fibrils. He concludes his paper with the very apposite statement: "We cannot suppose that this is a local phenomenon and that the peripheral nerves do not participate in similar alterations, and that the brain itself, composed in great part of tubular fibres, must be excluded. It is impossible not to anticipate important results from the application of this inquiry to the different nerves of the animal system, but it is particularly in reference to nervous diseases that it will be most desirable to extend these researches." How much light the extension of these researches during the last sixty years has afforded to neurology can be best appreciated by reviewing the enormous strides which have been made in our knowledge of the anatomy, physiology, and pathology of the nervous system. Waller had anticipated that degenerative processes would be found to occur in the central nervous system as well as in the peripheral nerves; and very shortly, in 1852, Türk described secondary degeneration of the spinal cord after a transverse lesion, and in 1854 he published his classical paper on secondary degeneration of tracts in the spinal cord and their prolongations in the brain, based upon 21 cases. As Waller's observations form the basis of our knowledge of secondary (Wallerian) degeneration of the peripheral nervous system, so Türk's observations constitute the foundation of our knowledge of secondary degeneration of the central nervous system.

Waller in 1852 extended his researches and formulated the three following fundamental laws: (i.) As a general rule the sensory fibres develop by starting from the peripheral and radical poles of the ganglion-corpuseles, and extend from these into the peripheral organs and in the spinal cord to a height undetermined. (ii.) The ganglion-corpusele is in consequence the central organ for the formation and nutrition of its peripheral and central branches, and accordingly we shall call it the neuro-genotrophic corpusele and the neuro-genotrophic body. This foreshadows the neuron doctrine about which a great deal more will be said shortly. (iii.) Considering the ganglion in its simplest state as a bipolar corpusele, we are able to assert that every part of the radical and peripheral poles which is separated from the corpusele becomes disorganised, whilst the whole of the poles in connexion with the corpusele remain normal.

It is generally admitted that this law formulated by Waller, although fundamentally true, requires modification. Dr. W. H. Dickinson, in an interesting paper on "The Changes in the Nervous System which follow the Amputation of Limbs," stated as a result of his observations, that the posterior roots may atrophy though still in connexion with the ganglia,



and the anterior roots likewise, though still in connexion with the spinal cord; and it appears that long disuse of a nerve is sufficient to lead to its atrophy, although those structures which immediately regulate its nutrition are complete. The degeneration described by Waller and Türk are degenerations secondary to injury, that described by Dickinson and numerous other observers since may be regarded as a *disuse atrophy*. Von Gudden in 1882 commenced his celebrated work upon atrophy of the cells of origin of a nucleus by tearing out the nerve in young animals; this method threw great light upon the origin of the cranial nerves, and was adopted with striking success by von Monakow and Forel.

In 1871 Gerlach, by the gold method of staining, shewed an intricate network in the grey matter; he came to the conclusion that the protoplasmic processes of the nerve-cells were all connected in a delicate network, and that out of this network strands of fibrils joined together to form fibres which passed out of the posterior roots and became sensory nerve-fibres. For fifteen years this doctrine was accepted, then Forel pointed out the limitation of secondary degeneration, and by the Gudden atrophy method shewed that degeneration or atrophy did not pass beyond a cell-station when the fibres which arise from these cells are cut through. He also called attention to the remarkable work of Golgi; while recognising the great value of the chrome-silver method, he opposed the interpretation of Golgi that this method proved the existence of a diffuse nerve-network; and argued that it demonstrated that the nervous system consisted of independent nervous units. We are thus led to consider the present position of the neuron doctrine formulated by Waller, revived by Forel, and reintroduced in the following terms by Waldeyer: A neuron is a nerve-cell and all its processes, including the protoplasmic processes or dendrons and the single axis-cylinder process with its cone of origin, its collaterals or side branches, and its terminal arborisation.

The *neuron doctrine* is that the nervous system consists of innumerable anatomically independent nervous units in contiguity but not in continuity. There is interlacing of the processes but no network. The nervous units are genetically and trophically independent cellular organisms arranged in functionally correlated systems, communities, and constellations.

It is admitted by all that the nervous system consists of nerve-fibres and nerve-cells supported by neuroglia, and the main point of discussion has been the origin of the nerve-fibres. How is the nerve-fibre formed? The answer given, first by Schwann and later by Balfour, Dohrn,<sup>1</sup> and many others, and still more recently by Apáthy, Bethe, and Schultze, is that the nerve-fibre is the product of a chain of cells, which extends from the nerve-cells to the peripheral termination; they assert that these sheath-cells secrete the fibrillae within their protoplasm. According to this view each interannular segment represents, not a cell pierced by a monstrous central heterogeneous prolongation, but a single cell highly

<sup>1</sup> Dohrn recently accepted the neuron doctrine.

differentiated. Certainly such an interpretation of the histological appearances could not be refuted till new methods of staining and of experimentation were adopted to disprove this statement.

His, by his embryological researches, on the other hand, concluded that the axis-cylinder and the other processes of the nerve-cell were the outgrowths of the cell protoplasm (Fig. 22). Then came the chrome-silver



FIG. 22.—Cross-section through the medullary cord of a salmon embryo, to shew neuroblasts and motor nerve-fibres (m.n.). (After His.)

method of Golgi, which, in the hands of Ramón y Cajal, Kölliker, Retzius, Lenhossék, van Gehuchten, and others, apparently demonstrated that the whole nervous system consisted essentially of independent anatomical units, and that the cylinder-axon was an outgrowth of the nerve-cell. Ramón y Cajal was able to follow the development of the neuron from the neuroblast in all its stages, from the first appearance of the short nervous process up to the long outgrowth which formed the nerve-fibre (Fig. 23). His researches extended over the most varied motor and sensory regions

of the central as well as of the sympathetic nervous systems, and fully confirmed the researches of His. These results of Cajal were soon followed by the important work of Held, who demonstrated that the nerve-fibre is an outgrowth of the nerve-cell, and accurately followed the origin and further development of the neuro-fibrils. They are situated, as His, Besta, and Lenhossék had already observed, in the interior of the neuroblastic protoplasm, first in the form of a loose skein, and then they grow out from the nerve-cell body into the nerve-process. Held, however, like Hensen, finds that the nerve-processes are not free, but grow into preformed tracts, which Hensen calls intercellular bridges (Fig. 24), and he further believes that instances may arise in which the neuro-fibrils of one

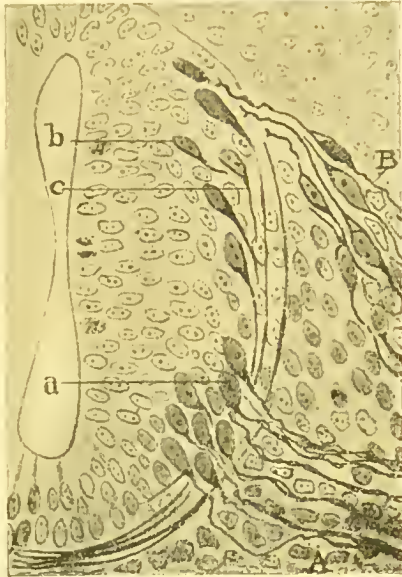


FIG. 23.—Section through a chick embryo of three days. A, motor root; B, spinal ganglion; a, motor neuroblast; b, c, commissural neuroblasts. (After Ramón y Cajal.)

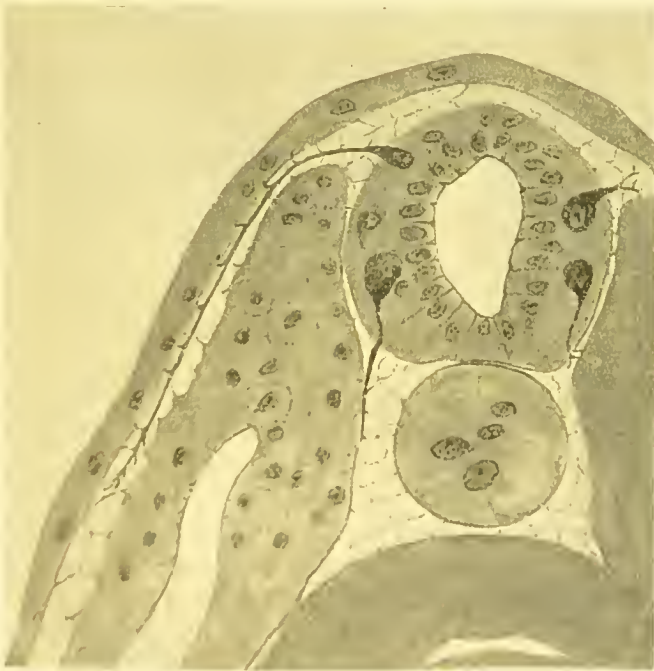


FIG. 24.—Semi-diagrammatic section through the spinal cord and adjacent organs of an axolotl embryo. The peripheral nerve-fibre is seen arising from the ganglion-cell; it does not grow out free into spaces between the cells, but into protoplasmic bridges or plasmodesmata which have been already formed by other cells. According to this hypothesis the nerve-paths arise through the transformation of these plasmodesmata into neurilemma. (After Held.)

cell grow into another cell, and commingle with the fibres of that cell passing out of its axon-process. As Verworn remarks, these are interesting histological details, but have no bearing on the neuron doctrine.

A glance at the figures (22, 23, 24, 25) given by the neuronists and the anti-neuronists explains why this different interpretation of the mode of development of fibres should occur. Ross Harrison truly remarks that it is impossible to decide by microscopical examination of sections of embryos whether the spindle-shaped cells lying around the nerve-fibres form the fibres as maintained by Bethe and others (Fig. 25), or whether they simply ensheath processes of the nerve-cells.



FIG. 25.—Cross-section through a chick embryo of seventy-three hours, to shew the beginning of a spinal nerve (sp.n.); m.c., medullary cord. (After Bethe.)

Harrison's observations upon the normal development of the salmon and frog led him to a decided opinion in favour of the neuron conception, but the attitude of the opponents of the doctrine was such that the study of normal development would never prove convincing—consequently he set about finding some means of differential experiment. Profiting by the knowledge of the transplantation experiments in tadpoles of Born, Ross Harrison planned a new and exact method of study—namely, the removal in turn of each of the two structures in the developing embryo-frogs (Fig. 26). Embryological studies had already shewn that the source of the sheath-cells was the ganglion-crest; accordingly he removed this structure in the embryo *Rana esculenta* before any differentiation of nerve-cells and -fibres had occurred. The dorsal portion of the medullary tube and the ganglion-crest were removed, and the embryo



was thus left with its nervous system as an open groove in its back, the walls of which contained the cells which would subsequently develop into the spinal motor-cells. Two embryos so operated upon were joined back to back, so as to prevent regeneration-processes vitiating the result (Fig. 26). These animals were allowed to live a certain time and grow; they were then killed and examined carefully by serial sections. No spinal ganglia or sensory nerves were found, and, what was of great interest, the motor nerves were found as fine protoplasmic threads extending from the spinal cord without a single sheath-cell around them

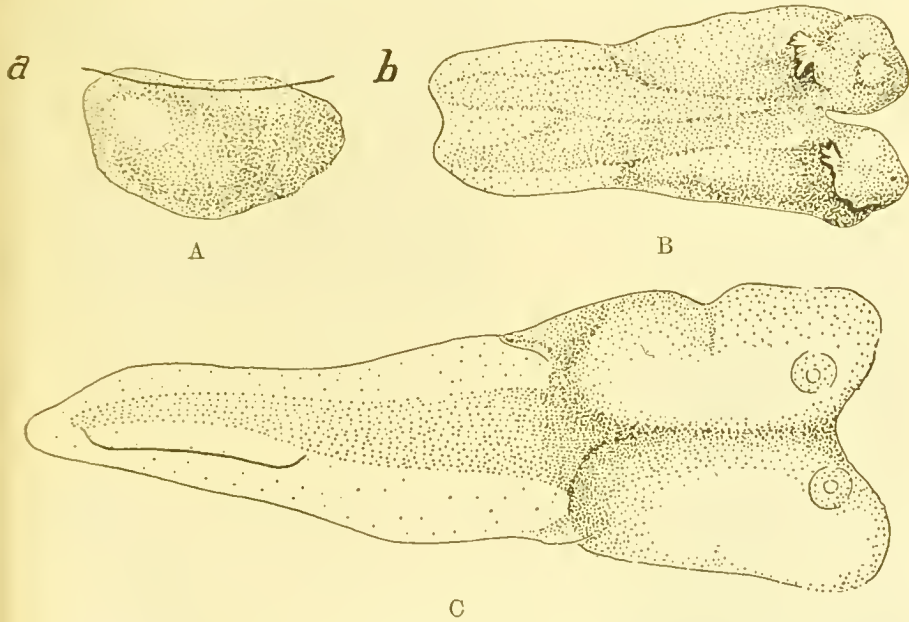


FIG. 26.—A, frog embryo, 2.7 mm. long. The line *a-b* indicates the incision for the removal of the ganglion-crest; B, C, two double embryos, from each of which the ganglion-crest has been removed, —B, two days after operation; C, six days after. (Ross Harrison.)

(C, Fig. 27). The nerve consisted simply of delicate fibrils. This experiment shews that the ganglion-crest forms the posterior spinal ganglia, the sensory nerves, and the sheath-cells. The conclusion is that the ganglion-cells can form the nerve-fibres without the aid of the sheath-cells. The next question Harrison sought to answer—and it is complementary to the last—was this: Can sheath-cells without ganglion-cells form the nerve-fibres? He made the same incision as before, but instead of removing the ganglion-crest he lifted it up and replaced it after removing with a fine-pointed glass pipette the remainder of the medullary tube. The embryo developed normally, but remained almost motionless; subsequent examination shewed that the sensory fibres and the sheath-cells appeared, but no motor-fibres; although normally the motor and sensory fibres run together, and this would allow the fibres to the muscles ample opportunities of developing from the sheath cells if the

latter were really the source of the motor fibres (1), Fig. 27). He found, however, that nerves separated from their cells of origin degenerate rapidly, and no signs of regeneration were observed.

The question may be asked, Does the ganglion-cell process extend as

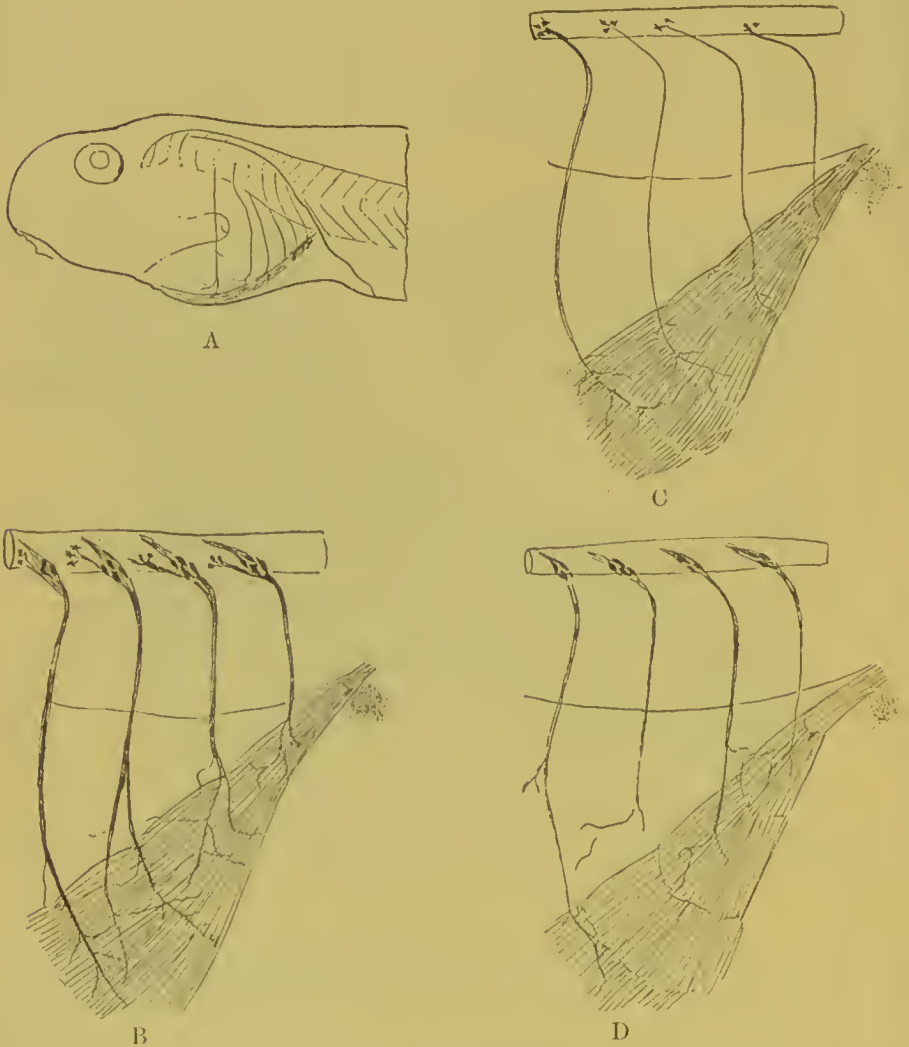


FIG. 27.—Diagrammatic views of the nerves in the abdominal walls of the tadpole. A, the body of a larva shewing general arrangement of motor and sensory nerves, surrounded by sheath-cells; B, arrangement in normal larva; C, arrangement in larva from which ganglion-crest has been removed, only the motor nerves shewing without sheath-cells; D, arrangement in larva from which the ventral half of the spinal cord has been removed, shewing only sensory nerves surrounded by sheath-cells. (After Ross Harrison.)

a nerve-fibre to its peripheral termination? or is this process, as Hensen maintains, a differentiation of protoplasmic connexions already in situ? This view of Hensen, according to which protoplasmic bridges are supposed to be left between the dividing embryonic cells, has been supported by the difficulty of conceiving how it is possible for a nerve-fibre

to grow out a long distance (and always to arrive at the right place), as,

for example, in the case of regeneration of the nerves of the foot after division of the sciatic nerve. Harrison sought to solve the problem thus: He cut out the medullary groove, that will form the spinal cord of an embryo, before there was any trace of cell differentiation, and placed a small piece of it in lymph removed from the lymph-sac of a frog; the preparation



FIG. 28.—Portion of a horizontal longitudinal section through the spinal cord, (m.c.), and portion of two muscle-plates (m.y.), of a frog embryo. The cell (n.), with the branched process is a neuroblast, shewing the first stage in the formation of a nerve-fibre. (Ross Harrison.)

was put on a cover-glass, and mounted on a hollow slide and sealed with paraffin. The lymph clots almost immediately and holds the transplanted tissue in place. He has kept preparations alive in place. He has kept preparations alive five weeks and watched the development of the neuroblast, and he has seen the axon develop and grow. A somewhat similar structure to the cone of increase described by Cajal by his silver method of staining embryonic spinal cords (see B, Fig. 31) can be seen. Probably it is also similar to the terminal bulb of regenerating axons found in the proximal stump of a divided nerve. Harrison has observed a growth of  $20\ \mu$  in twenty-five minutes as shewn in figure 30. Control experiments with other tissues of the embryo gave no such results. These remarkable observations of Ross Harrison shew beyond question that the nerve-fibre begins as an outflow of hyaline protoplasm from cells situated within the central nervous system. This protoplasm is actively amoeboid; retaining its pseudopodia at its distal end, the protoplasm is drawn out into a thread

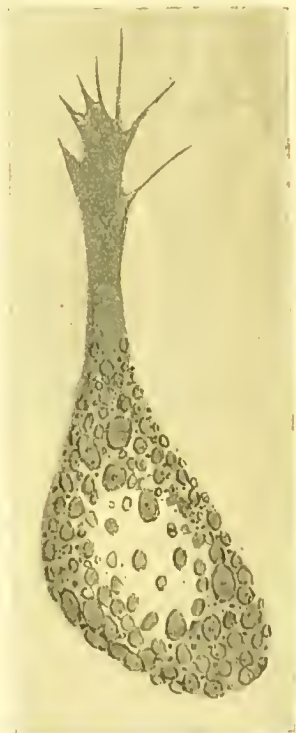


FIG. 29.—Isolated cell from a piece of embryonic spinal cord, growing in a drop of clotted lymph. The cell-body, which is filled with yolk-granules, is sending out a hyaline protoplasmic process which undergoes amoeboid movements. Drawn from a living specimen. (Ross Harrison.)

which becomes the axis-cylinder of a nerve-fibre. Although Harrison has disproved the hypothesis that the sheath-cells form the essential portion of the nerve, namely, the axis-cylinder, yet he fully admits, as all those who uphold the neuron doctrine do, that the cells of the sheath of Schwann play an important part in the nutrition and production of the nerve-fibre. These experiments of Harrison place the outgrowth doctrine of His on the safest of all foundations, namely, that of direct observation. It is, moreover, interesting and important to note briefly that Marinesco, Goldstein, Minea, and Nageotte have observed in transplanted spinal and sympathetic ganglia of warm-blooded and cold-



FIG. 30.—Two views, taken at twenty-five minutes interval, of the same nerve-fibre growing from a group of embryonic spinal-cord cells into the lymph. (Ross Harrison.)

blooded animals an outgrowth of fibrils from the ganglion-cells. As Verworn truly says, the embryological basis of the neuron doctrine has been established beyond dispute. The formation of connexions of one neuron with another by fibrils, the passage of fibrils from one nerve-cell through another nerve-cell are matters of detail which in no way shake the fundamental principle of the neuron concept, namely, that the cell and its processes form a nerve-unit which has a genetic independence. According to Kölliker, all the nerve-fibres arise from nerve-cells of the central nervous system and the ganglia. The peripheral nerve-fibres are surrounded by special cells, constituting in the adult the sheath of Schwann. The latter appear when the axis-cylinder is developed, and constitute for it a superficial envelope. These sheath-cells all arise from the mesoderm and multiply by karyokinesis. According to Frobiep,



however, the cells of the sheath of Schwann of the peripheral nerves are probably, like the neuroglial cells, of ectodermal origin. Certainly Harrison's experiments seem to support Froiep's views.

The anatomical observations of Cajal and others regarding the genetic independence of the neuron have thus been fully confirmed by the researches of Harrison. The next question is, are the sheath-cells of no further use than to enclose the axial core; in fact, is there a complete trophic independence of the nerve-cell and its processes?

Experimental and clinico-anatomical observations indicate that the sheath-cells play an important part in regeneration after injury of the axon. To prove this statement we have only to consider the difference in the results on the extra-medullary and intra-medullary course of the axons of the posterior spinal ganglia after section of the posterior roots. Prof. Sherrington and many other observers have described fine medullated regenerated fibres around the cord—that is, central to the seat of injury—but only isolated observations have shewn a few regenerated fibres in the exogenous systems

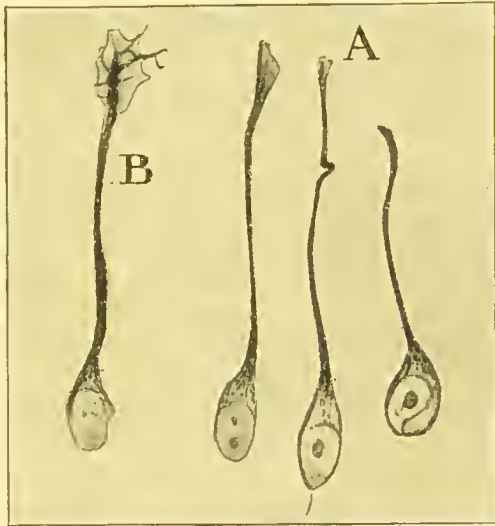


FIG. 31.—A, Neuroblasts stained with nitrate of silver; B, neuroblast impregnated by the Golgi method. Growth-cone appears well marked at the top of B. (Ramón y Cajal.)

of the posterior columns. Again, although Marinesco, Minea, and Fickler have seen attempts at formation of regenerated fibres after transverse lesions of the spinal cord, there is no restoration of function, because there is no re-establishment of connexion with the appropriate neurons. We may correlate these facts with the presence of sheath-cells in the extra-medullary posterior roots and the absence of the same in their intra-medullary course. Simple section of the nerves, as Nissl, Marinesco, van Gehuchten, and others have shewn, produces chromatolytic changes, but as a general rule the cells do not undergo atrophy. It may be assumed that evulsion of cranial nerves, as practised by Gudden (*vide* p. 175), was a more serious injury, and destroyed not only all the sheath-cells of the neuraxon up to the point of origin of the nerve from the central nervous system, but was also a much more serious injury of the neuraxon itself.

Before proceeding to describe the recent advances in our knowledge concerning the changes which take place in the proximal and distal ends of a divided nerve, it will be well first to consider the changes in the nerve-cells of origin as revealed by the Nissl method.

**Changes in the Cells due to Lesions of Cranial and Peripheral**

**Nerves.**—Nissl first published (1892-94) detailed accounts of the changes in the nerve-cell (observed by his method of staining), produced by section of the nerves. Twenty-four hours after section of the facial nerve in the rabbit there is a reaction in the cells of the facial nucleus. The chromatic substances commence to disappear in limited regions of the cell body, and after two days instead of presenting the blocks of stainable substance, now known as the Nissl granules, there was observed a fine dust of coloured particles. By the third day the process had extended to the dendrons. At the end of five or six days the cell has changed its form, it has become rounder, the prolongations less visible, and the protoplasm looks as if sprinkled with dust-like particles of stainable substance. During this time the nucleus has altered its position and become eccentric. Nissl also studied the alterations in the cells of the posterior spinal ganglia produced by section. Marinesco repeated and confirmed Nissl's experiments, using the hypoglossal nerve. He was followed by Ballet and Dutil, Lugaro, van Gehuchten, Flemming, and many others. The changes observed may be thus summarised: Swelling of the cell body with slight increase of volume of the nucleus and of the nucleolus, the cell becomes rounder and the prolongations in their turn swell; there is disintegration of the Nissl granules, a process which begins in the central region of the cell near the axon-cone of origin. The first changes are observed twenty-four hours after section, and they progress until the whole perinuclear region exhibits this chromatolysis and the Nissl granules on the protoplasmic processes disappear. The nucleus becomes eccentric in proportion to the amount of chromatolysis. These changes are due to alterations of the osmotic conditions of the cell caused by the injury to its axon-process, whereby fluid is absorbed from the ambient medium. Marinesco names this characteristic change perinuclear chromatolysis; a similar appearance of the nerve-cells is seen in neuritis. I have observed it in all cases of alcoholic polyneuritis and in lead neuritis. This reaction of injury to the nerve-cell when its axis-cylinder process is injured is in direct confirmation of the correctness of the neuron doctrine, for if the sheath-cells formed the axon it is much less likely that the nerve-cell would shew such changes, which may even proceed to their atrophy and disappearance. It is remarkable that when a nerve is divided some only of the motor spinal ganglion-cells are so severely damaged that they do not recover, but undergo atrophy and disappear; so, too, in polyneuritis some cells hardly shew any change, whilst others are so injured as to be incapable of recovery, and eventually atrophy and disappear. Again, in transverse lesions of the spinal cord, as shewn by Pusateri, Marinesco, and Gordon Holmes and Page May, the Betz-cells of the cortex undergo similar chromatolytic changes which may proceed to atrophy, but the cells are affected very unequally, for we may observe two Betz-cells lying side by side, the one seriously damaged and the other hardly affected at all. Drs. Sewell and Turnbull have investigated a case of transverse lesion of the spinal cord due to fracture of the spine

at the level of the fifth cervical. The boy died eight weeks after the injury. The Betz-cells at the top of the ascending frontal convolution shewed all degrees of chromatolysis, from cells with hardly perceptible changes to complete disappearance of the Nissl granules.

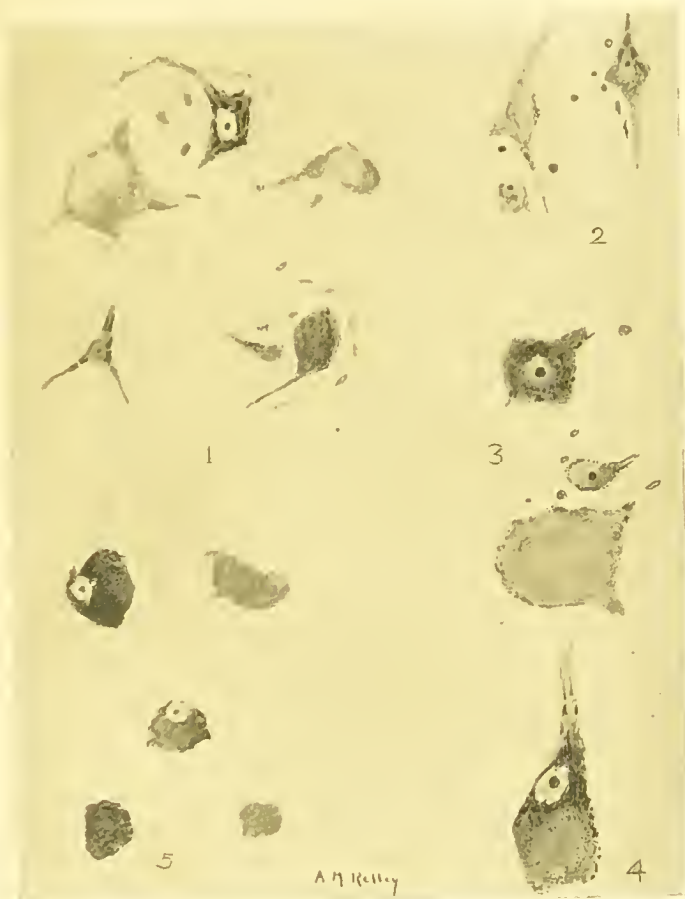


FIG. 32.—(1) Group of anterior-horn cells from a monkey's spinal cord on the side on which section of the sciatic nerve had been performed. On the opposite side hemisection and section of all the lumbosacral roots had been performed, in addition to section of the sciatic nerve. Yet there were as many altered spinal motor neurons on the one side as on the other, thus shewing that the cause of this alteration was the section of the nerves, and that interference with the passage of stimulus had had little to do with the trophic condition of the cells. It will be observed that some cells have the normal Nissl pattern; (2) Cells of the cortex cerebri in phosphorus poisoning of the rabbit. It will be observed that one cell shews considerably more chromatolytic change than the other; (3) Cells of the anterior horn of the cervical enlargement in a case of peripheral neuritis caused by chronic lead-poisoning. The perinuclear chromatolysis and eccentric condition of the nucleus are very evident, and the appearance presented is the same as by the large cells in (1); (4) A large Betz-cell of the cerebral cortex with eccentric nucleus and chromatolysis specially marked around the axon-cone of origin; from the same case of lead neuritis; (5) Five cells shewing various degrees of eccentricity of the nucleus and chromatolysis of the posterior spinal ganglion-cells; from a case of alcoholic neuritis.

I have observed also in experimental poisoning by botulin, absinthe, phosphorus, and other poisons, also in acute and chronic poisoning of human beings, that the neurons are not equally affected. Still more striking is the fact that, after experimental ligation of all four

arteries, 2 carotids and 2 vertebrae, or 2 carotids, 1 vertebral, and 1 subclavian, whereby an experimental cortical anaemia in lower animals, for example, monkey, cat, and dog, was produced, the cells of the same type, namely, the Betz-cells, were not equally affected; relatively a few only were so damaged as to undergo destruction. The conclusion is that the specific vital energy of some cells is greater than that of others, just as the individuals of a society are not all possessed of the same vital resistance to injury or poison; but as we know that the vital resistance of the individuals of a society is largely a matter of nutrition, fatigue, and powers of conservation of energy, so probably is it with the neurons. Those in which nutritional equilibrium is in a low state, either from inherent defect, fatigue, or other causes, will suffer most.

I have also observed very well marked chromatolysis of the Betz-cells in cases of chronic alcoholic and chronic lead polyneuritis; it was more marked than could be accounted for by the small amount of degeneration of the pyramidal tracts, and I cannot help thinking that it was the effect of the poison on the whole system of efferent neurons concerned with reflex and voluntary movements plus the parenchymatous and peripheral interstitial polyneuritis. All the neurons, however, do not undergo destructive atrophy; probably only those in which the nucleus is extruded are incapable of recovery. In my experience even in severe cases of polyneuritis recovery may result from continued passive movements of all the joints and massage of the muscles. The avoidance of pressure and weight of the bed-clothes in rendering a foot-drop permanent; the instruction of the patient to make voluntary effort by aid of attention and vision, and to try to assist the operator in making the passive movements; the placing the feet against a board while lying in bed, and the daily placing the feet on the ground in the effort to feel the weight of the body supported by the limbs, all tend, by favouring incoming and outgoing stimuli, to open up the old paths or to restore function by new paths. This is no mere hypothesis, for it is based upon Mink's observation that monkeys, in which the motor area had been removed much more completely, regained movements when placed in a cage large enough to enable them to spring about and take free exercise.

Upon this assumption, therefore, that stimulus exercised an important influence upon regeneration of nerves, Prof. Halliburton and I carried out a series of experiments to see if regeneration of the motor nerves was interfered with by cutting off, so far as we were able, stimuli from the spinal motor neurons of a limb. We adopted the following procedure: Unilateral section of the posterior roots from the third cervical to the third dorsal inclusive was performed on monkeys. There was as a result a marked hypotonus of the limb, which hung useless as a flail, and the animal did not use it for purposive movements. We then divided and sutured either the median or the ulnar nerves on the two sides. There was, apparently, no difference in the time taken for regeneration on the two sides, nor could we discover any more marked changes in the anterior-



horn cells of one side than of the other. Again, the motor area of the right side of the brain was removed in an animal in which the same posterior roots had been divided; the nerves were divided on both sides, and the result was the same as in the previous experiment. A third experiment was performed: a unilateral section of the lumbosacral roots was combined with hemisection of the spinal cord in the mid-dorsal region, and both sciatics were subsequently divided and sutured. Even in this experiment we could not state that all sources of stimulus to the spinal motor neurons of the side of the double lesion had been removed. Still, the greater part of the paths exercising any influence upon the discharge from the spinal motor neurons had been removed, and if stimulus really did play an important part in the nutritional activity necessary for regeneration of the motor nerves, after section of the axons of the motor neurons, it might be certainly expected that regeneration would be delayed on that side; but it was not, and this accords with the fact that the characteristic changes in the ganglion-cells were not more apparent on the side of the double lesion than on the opposite side. A careful examination of sections of the spinal cord failed to shew more ganglion-cells presenting chromatolytic changes on one side than the other. In order to avoid any personal bias, I tried to see if I could ascertain on which side the double lesion had been made by an examination of the anterior horns; but I failed entirely, although when I shifted the specimen, so that the posterior cornua came into the field, it was quite evident from the atrophy of the fibres and changes in the cells. Fig. 32 shews two degenerated cells on the side opposite to the spinal and root lesions.

The trophic activity of the spinal motor neurons is therefore in all probability independent of stimulus arriving from other neurons. They possess, indeed, a trophic autonomy. The observations of Harrison, already alluded to, support this idea; moreover, he "has shewn that amphibian embryos reared in a solution of acetone-chloroform acquire a perfectly formed nervous system, and one capable of normal functional activity, though during the whole period of their development up to the stage when the yolk is entirely absorbed (at which time the peripheral nerves are all well developed), no functional activity of the nervous system is manifested." This accords with the neuron doctrine of genetic and trophic independence. Direct injury of any part of the neuron will cause changes but not injury of neurons with which it is functionally but not nutritionally correlated.

The axon consists of a number of conductible fibrils, and the more of these fibrils that are severed the greater will be the injury to the neuron. It is possible that fibrils constituting an axon may not come entirely from one cell in every case; there may be, as Held suggests, in some instances a commingling of fibrils to form the axon of a nerve; in such a case it is conceivable that the reaction of injury would be less than when all the fibrils of a cell are divided.

We have briefly discussed what happens to the cell when that portion of the neuron which is termed the axon is injured; I will now consider

the changes which occur (*a*) in the proximal end of a divided nerve, and (*b*) in the distal portion of the nerve, in the light of modern researches, especially as revealed by the silver method of Cajal, which shews that a neuron consists of fibrils which pass from the dendrons through the body of the cell to the axon, and consequently may be assumed to act as the conductible element of the neuron.

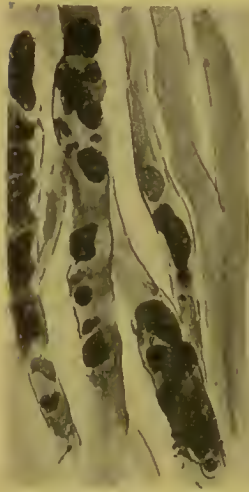


FIG. 33.—Wallerian degeneration of regenerated nerve-fibres in a cat. Marchi method of staining. (Magnification, 600 diameters.)

The appearances presented by fibres undergoing degeneration when stained by the Marchi method are illustrated by Fig. 33. I wish, however, to call attention to Fig. 34, which is of considerable interest for another reason to which I will briefly refer. The following experiment was performed by Prof. Halliburton and myself. A small piece was resected from a nerve in which regeneration had taken place, and histologically the nerve was shewn to possess many fine myelinated fibres. Ten days later the animal was killed, and the portion of the nerve below the resection was examined; no myelinated fibres were found, but a number shewing Wallerian degeneration.

If the sheath-cells had been mainly instrumental in the formation of the new regenerated fibres, resection of the piece of nerve should not

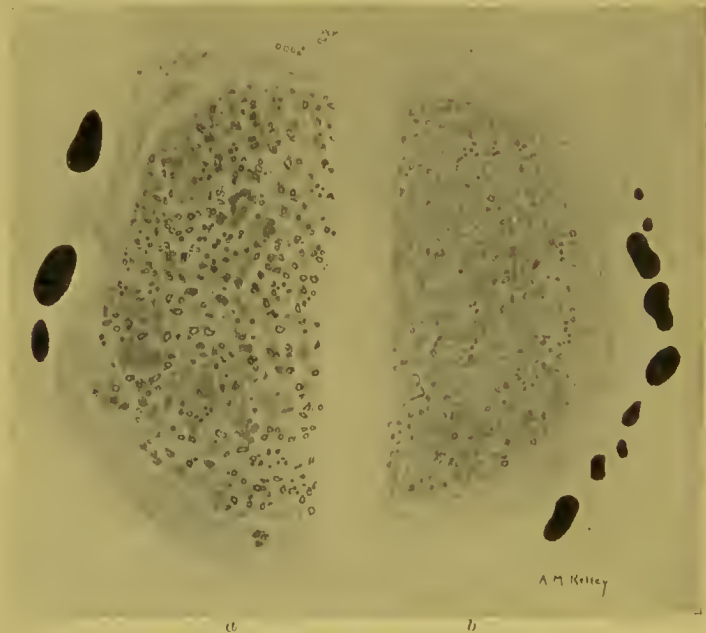


FIG. 34. (*a*) Regenerating motor bundle of a cat's sciatic nerve, ninety-one days after the nerve was divided and sutured. Marchi's method of staining. The transverse section shows well-marked myelination in the majority of the fibres; it was taken from the upper end of the nerve. (Magnified 220 diameters); (*b*) The same bundle 3 in. lower down. Myelination much less advanced. (Magnified 220 diameters.)

have had any influence upon the nerve which had developed from the sheath-cells.

**Changes in the Proximal Cut End of a Nerve.**—The changes which occur in the proximal end of a cut nerve were very incompletely known before Cajal introduced his silver method, and the histological observations of Perroncito, Cajal, and Marinesco by this method have thrown a new light upon the process of regeneration. Perroncito, three hours after section of the nerve, has found in the proximal end of the nerve very fine collateral ramifications of the axon, terminating, after a short course, in very delicate filaments. After eighteen hours he has observed in the



FIG. 35.—Regenerating nerve-fibres from the proximal end of the sciatic of a dog, six to forty-eight hours after cutting the nerve. (Perroncito.)

proximal end most of the anatomical conditions indicative of regeneration, which, previous to his researches, had been looked upon as late productions of the axis-cylinder—namely, the plaquette, the ring, the button, and the helicoidal formation (Fig. 35). These observations of Perroncito shew that active nutritive changes commence almost directly after the injury, before the sheath-cells divide. Marinesco has confirmed the observations of Perroncito, and has found that within twenty-four hours of section of the sciatic nerve very important and interesting phenomena of regeneration occur. These phenomena are the results of an increased nutritive activity associated with a swelling and hypertrophy of the large axis-cylinders, whereby the constituent nerve-fibrils which make up the axons become evident. The network or skein of fibrils are clearly seen, owing

to a great increase of the interfibrillar substance, and a longitudinal dissociation of the bundle of fibrils takes place. These skeins of fibrils may run side by side or intercross one another. The various appearances of the fibrils resulting from this longitudinal dissociation are represented in the figures, and are very different from one another. Between the tangled skeins of dissociated fibrils there may be off-shoots of more delicate fibrils forming plexuses (Fig. 36). Some of these delicate fibrils



FIG. 36.—Sciatic nerve of a dog, five and a half days after section. Details of degeneration in the proximal end. A, axis-cylinder with a nearly normal appearance in its upper part, whilst in its lower part it is considerably swollen, and the neuro-fibrils are very apparent, and like a tress of hair. In reality it is a reticulated structure made evident by an increase of the interfibrillar and periaxonal substance; B, axis-cylinder swollen and with the neuro-fibrils dissociated at the upper part, and reunited in diverging cords towards the upper third. Some of these end in a terminal bulb; C, the axis-cylinder swollen in a still more marked manner, and consisting above of tresses of neuro-fibrils. These reunite into cords below, which more or less surround the debris of a degenerated axis-cylinder. (After Marinesco.)

terminate in a little olive or cone of growth (Fig. 37). This process of longitudinal fibrillar dissociation of the axon leads to the formation of a number of embryonic fibres, from which develop a number of young axis-cylinders. These young fibres can be followed through the proximal cut end to the cicatrix. Some are seen to terminate in a button-, olive-, or club-shaped extremity, forming a cone of growth which penetrates between the more or less longitudinally arranged sheath-cells (Fig. 38). At the termination of the cut ends there is a cellular exudation and new-formed blood-vessels; this undergoes organisation, and at the end of six or seven days forms a bridge which unites the two cut ends for the passage of the



young regenerating fibres. But in proportion as the axon-fibres penetrate the cicatrix they diminish in number and their branches are less numerous. The new fibres may be seen to diverge, intercross, and form a felt-work (Fig. 39). A certain number of them, however, can be seen taking a straight course and descending vertically in the peripheral stump. Cajal considers that the terminal bulbs correspond to the cone



FIG. 37.—Olive-shaped swellings at the end of nerve-fibres, growing downwards from the proximal end, twenty-one days after section of the nerve. Coiled-up fibrils can be seen in those swellings. (Marinesco.)



FIG. 38.—Regenerating nerve-fibres of a cut nerve. The young fibres, a, b, c, d, e, growing from the proximal end, can be seen passing through the cicatrix down into the distal portion between the proliferated sheath-cells, some of these are seen to bifurcate, for example, d, c, e. One branch of d terminates in an olive-shaped bulb, f, the other proceeding onwards. It is possible that the former is arrested in its progress, and coils up to form the olive. (Ramón y Cajal.)

of growth of the developing axon in the embryo or pseudopodia in the advancing axon of the neuron observed by Harrison in his experiments (Fig. 30). Probably Cajal is correct in maintaining that the terminals of the new-formed young fibres correspond to an amoeboid phase of very active growth, which assures the neurotisation of the distal end of the divided nerve. After the stage of active ramification or dendro-amoeboidism numbers of terminal clubs of the young fibres are seen.

These traverse paths rendered free to their passage between the sheath-cells. Marinesco thinks that these terminal clubs only indicate a delay or retardation of chemiotropism of the sheath-cells. The shape of these terminal bulbs, which are so striking a feature of the regenerating nerve-fibrils, is variable; in structure they consist of a network or twisted skein of fibrils in the form of an olive or bulb, and an interfibrillar amorphous substance (Figs. 37, 40). It is difficult to decide



FIG. 39.—Longitudinal section of the sciatic nerve of a dog, eight days after section. A, proximal end; B, Cicatrix; C, distal end. (Marinesco.)



FIG. 40.—Hypertrophied fibres of the proximal cut end of a nerve with very obvious fibrils presenting an abundant lateral and terminal division. Some of the collateral and terminal ramifications are seen ending in a small or large bulb; others have a free extremity. The proliferated sheath-cells are very obvious. (After Marinesco.)

whether these bulbous terminals represent cones of growth or a twisting up of a fibril on account of an obstacle to the growth or nutrition of the nerve fibril.

In sections made of the junction of the proximal and distal ends at successive periods of time, three stages can be seen: (i.) The sprouting of large numbers of new fibres from the proximal cut axon; (ii.) the penetration of the bridge of young vascular connective tissue joining the cut ends by the young nerve-fibres; and (iii.) the penetration and growth downwards of these young fibres between the proliferated sheath-cells of the peripheral portion (Figs. 38, 39, 40). There can be no doubt, then, that

the new nerve-fibres depend upon an outgrowth from the proximal cut end of the neuraxon.

What part, then, we may ask, do the sheath-cells play in regeneration? In answering this question it is well to consider some of the appearances presented by the peripheral fibres which are undergoing Wallerian degeneration when stained by the Cajal silver method. The lesions are the same in all animals, but the moment of their appearance depends upon the species and age of the animal, and on the severity of the injury which has caused the solution of continuity of the nerve. The changes appear first at the upper end, and are propagated peripherally through the whole extent of the nerve below the lesion. The degeneration does not affect all the fibres equally. The first change is a swelling of the axis-cylinder whereby the fibrillar network is displayed. The neuro-fibrils are visible and appear thickened in their course. But very soon the axon appears only as a dark-stained finely-granular cord (A, Fig. 41). In place of the neuro-fibrils there is a dark mass of fine granules. Marinesco terms this condition "axolysis." Resorption occurs in this softened and swollen axon, causing vacuolation (B, Fig. 41). The vacuolation becomes more marked as the process of resorption continues, and this results in fragmentation of the axon, and, finally, the fragmented axon is completely destroyed and absorbed.

**Degeneration in the Distal Portion of the Cut Nerve.**—Parallel with the lesions of the axis-cylinder there appears a breaking up of the myelin sheath into globular or ovoid droplets of various sizes. Marinesco believes that the fragmentation of the myelin sheath and of the axis-cylinder constitutes connected phenomena dependent upon the same cause, namely, the existence of digestive ferments on the inner surface of the sheath of Schwann. These ferments only operate when the axon is cut off from its trophic centre. Bokay has found that the pancreatic juice decomposes lecithin into glycerophosphoric acid, choline, and a fatty acid. In Wallerian degeneration the myelin breaks up into glycerophosphoric acid, choline, and a fatty acid (Mott and Halliburton). Consequently the chemical changes in Wallerian degeneration may be analogous to pancreatic digestion, and due to a proteolytic and lipolytic ferment. The sheath-cells undergo rapid proliferation, and exercise a phagocytic action upon the products of degeneration, while others arrange themselves in a longitudinal direction to receive and attract the rapidly growing young fibres which have come from the proximal cut end.

The experiments of Forssmann appear to shew that the products of degeneration have a chemiotrophic influence upon the developing fibrils of the proximal cut end of the nerve. Forssmann cut the tibial nerve and brought the proximal cut end into relation with the divided peroneal and tibial nerves which he placed in a celloidin tube; two months later he found the same number of regenerated fibres in each of the nerves. This may support the view that the sheath-cells exercise a chemiotactic influence, but Forssmann made another series of experiments shewing that this chemiotropism depends upon chemical attraction of the



degenerated myelin. His experiments were conducted thus: He divided the proximal end of a nerve and placed each half into separate celloidin tubes; one was filled with emulsion of liver and the other with brain emulsion; the fibres all grew in a direction towards the tube containing the brain emulsion. It may be concluded from this experiment that the degenerated myelin of the peripheral portion of the nerve attracts the young fibres and that the sheath-cells surround them.



FIG. 41.—Represents four fibres showing different degrees of axolysis. A, the axis-cylinder no longer shows the neuro-fibrils, but consists of abundant fine granules disseminated in the inter-fibrillar substance; B, formation of cavities and vacuoles in the interior of the axis-cylinder, in consequence of resorption of the granules; C, the same condition more advanced; D, fragmentation and breaking up into small pieces of axis-cylinder. (After Marinesco.)

Forssmann also shewed that the fibres of the proximal end do not take the line of least resistance, but the direction in which chemiotropism attracts them. Cajal, however, asserts that it is the attraction of the protoplasmic strands formed by the sheath-cells which are arranged in dense fusiform bundles; and Cajal and Marinesco believe that these neurilemmal cells secrete a chemiotropic substance capable of exciting amoeboid movement in the pseudopodia of the young regenerating axons, and having attracted, direct and nourish them. Marinesco considers that he has proved this by the following experiments. A

piece of dead resected nerve, in which the sheath-cells are dead, is taken; it was obtained either from a dead animal, or by resection from a living animal of a piece of nerve which was allowed to remain for a sufficient time in serum for death of the sheath-cells to have taken place. This was connected to the proximal cut end of the sciatic nerve of an animal. To the proximal cut end of the other divided sciatic nerve is connected a piece of resected nerve kept alive in Locke's oxygenated serum. In the former case, when the sheath-cells are dead there is no chemiotropic influence upon the fibres of the proximal cut end, whereas in the latter, if the resected nerve is from the same species, the fibres of the proximal end grow in. These facts accord entirely with the observations of Harrison, and shew that the neuron is stimulated to grow out; all the energy of the cell now is expended in growth; as the cell-processes grow down into the new sheath an interaction takes place between the new axis-cylinder and its sheath.



leading to the formation of intervening myelin. Moreover, Prof. Halliburton and I found, in regenerating nerves, as Fig. 34 shews, a much larger number of myelinated fibres and the myelin sheath of the fibres thicker near the point of section than in a remote portion of the nerve. This has also been observed by Prof. Langley and Dr. Anderson, and indirectly supports the outgrowth doctrine.

The question still remains, How are the neurons connected with one another; if they are independent, how are they functionally correlated? This has, from the foundation of the neuron concept, been a point in dispute. Although many valuable researches have been published, we are still far from understanding the problem. The Golgi method appeared to shew that the neurons are arranged in systems and communities in contiguity, but not continuity, and numbers of experiments and observations were made to shew that the dendrites exercised amoeboid functions; and little buds or gemmules on these processes of the cells were supposed to appear and disappear owing to the contractility of the protoplasm, thus leading to varying degrees of contact-influence of one neuron upon another. But there is no proof that these gemmules exist in the living cells, although the amoeboidism of the branching processes of the neurons does seem possible as an explanation, when Harrison's experiments combined with Perroncito's observations are considered. But, as Verworn justly remarks, we must be careful not to generalise upon insufficient data, for the physiological connexions in the nervous system of the lowest types of animals and of the higher vertebrates are extraordinarily different; take, for example, the simple reflex processes in the lower invertebrates and the complicated processes of association in the human being. In the invertebrates there can be no question that Apáthy and Bethe are right in asserting that there is a fibrillar continuum through several ganglion-cells, for example in the medusa; but then we know that in this animal a stimulus can travel in either direction, and is propagated to the whole ring, so that when one tentacle is touched the whole musculature is contracted.

But does a continuity exist in the vertebrates? In my Croonian lectures on the Degeneration of the Neuron, I referred in the following words to some important researches of Held which had been put forward to disprove the neuron doctrine:—"In my opinion, however, one can still accept the neuron theory and admit the truth of Held's observations, namely, that the terminal arborisation of the axis-cylinder process of one neuron forms protoplasmic conerescences by fusion with the cell body and dendrons of another. This, of course, implies continuity of the protoplasm of one neuron with another, but trophically and genetically the two are independent, and it is merely a question of degree of contact of the protoplasm of one with the other. Held agrees with other investigators that in embryonic tissues, and even in early life, the neurons are entirely independent of one another. This independence he can determine by a line of demarcation at the points of contact due to a difference in refraction. This refractive limiting line is, however, not demonstrable

in the adult, and he comes to the conclusion that during the process of growth the protoplasm of related neurons fuses." Verworn states that the pictures which Held publishes are not clear enough to satisfy him. On the other hand, the possibility is undeniable that where the axon of one neuron is in contact with the dendrites of another there is a "receptive substance," which Prof. Sherrington has termed the synapse; this substance may possess certain physiological properties which bear some similarity to those of the end-organ in striped muscle—for example, susceptibility to fatigue, great summation, capacity for excitations, and specific reactions for certain poisons. "But it remains undecided whether the acceptance of such a synapse having these physiological properties is necessary for the explanation of the physiological processes. In any case great difficulties exist both for the acceptance of the synapse and for the acceptance of a continuous path of conduction. It is undoubted that conduction of the stimulus through the reflex arcs only occurs in the physiological and not in the opposite direction. Yet it can be demonstrated that the nerve possesses conductibility in both directions; therefore the necessary conditions for this difference of conductibility must be in the centre. Where the conditions are situated and how they are affected, the future must decide." It is admitted that the lower we descend in the zoological scale the more obvious is the fibrillar continuum, and the simpler and less varied are the motor adaptations to environment. We may assume, therefore, that in the upward development of the animal series with the complexity and refinement of motor adaptation there coexists a neuronic independence. We may inquire, what would be the advantage of neuronic independence in the evolution of the nervous system? In the attempt to answer such a question it is desirable to look at it from a broad biological standpoint. What are the properties of nerve tissue, and how does it differ from other cell protoplasm? We may say it is irritable and conductible, but we know that the protoplasm of the carnivorous plants—the sundews and Venus' flytrap—is irritable, conductible, contractile, and secretory, and that these plants are capable of exhibiting reflex action without a nervous system when the appropriate stimulus is applied. This reflex action, however, differs from that of the plant-like animals with their diffuse network of neuro-muscular cells in speed of reaction. Consider, moreover, the advantage of speed of voluntary action initiated in the brain by the impulse having to pass through the conductible fibrils of only two nervous cells in the production of motor reactions of the arm, leg, face, and tongue. But if there existed a fibrillar continuum from the cerebral neuron through the anterior spinal neuron, how could the anterior motor spinal neurons form the "final common path" for a multitude of different muscular activities?

The notion that the neuraxon of a Betz psycho-motor cell is connected by its conductible fibrils with one anterior spinal motor neuron is a textbook myth which, instead of making the nature of voluntary movements clear, only raises the question, Are the number of fibres in the

pyramids of the medulla equal to the sum of all the fibres in the anterior roots? Clearly, then, the fibrils of the Betz-cells must be connected with a number of spinal motor neurons forming the final common path for a multitude of different voluntary muscular activities. Moreover, we know that there is not a direct connexion between the upper cerebral neurons and the lower spinal motor neurons, for intercalary neurons with axons which do not leave the grey matter intervene, and the terminal arborisation of sensory afferent neurons, cerebral and cerebellar efferent neurons, combine with spinal association-neurons through the intercalary neurons in augmenting and inhibiting the outflow of energy of the spinal motor neurons whereby the most varied, refined, and complex muscular reactions in adaptation to environment are effected. The linking together of neurons to form systems and communities with afferent-sensory, efferent-motor and secretory and association functions, will be considered later (*vide* p. 237).

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**CAUSES OF NERVOUS DISEASE.**—A correct comprehension of neuropathology necessitates the study of (i.) the causes which give rise to nervous diseases; these are often complex; (ii.) the changes in the structure and functions of the nervous system produced by these causes. The causes of pathological processes occurring in the nervous system may be divided into *internal* and *external*, but in nearly all cases, except those due to direct injury, the two are more or less combined.

**Internal Causes.**—The successful investigation of the causes of nervous diseases, especially those spoken of as functional which include all the paroxysmal psychoses and neuroses, will largely turn upon



our ability to ascertain what an individual is "born with," and what has happened after birth—"nature and nurture." Each case should be studied as a biological problem in which the satisfaction of the instincts, appetites, and desires plays the predominant part in the reaction of the individual to his environment, the perceptual and intellectual reactions being secondary and dependent essentially upon the particular social conditions relating to the preservation of the individual and the species. It is the just balance of the cognitive and affective conditions which is essential for a well-balanced stable mind.

Of all the causes of nervous disease, *hereditary predisposition* stands pre-eminently first. It may come directly from one or both of the parents, or from more distant ancestors; strictly speaking, it is the tendency to nervous disease and insanity rather than the disease itself that is inherited, and this is frequently spoken of as the "neuropathic tendency." There are a number of *inherited diseases* which affect members of a family, the disease frequently commencing in each individual at about the same age. These are termed "family" or familial diseases, for example, hereditary ataxia (Friedreich's disease), hereditary chorea, and various forms of idiopathic muscular atrophy, and amaurotic idiocy. Alcoholism and syphilis in the parents, especially if one or both come of a neuropathic stock, frequently engender, by the production of defects in the germinal plasm, arrest, imperfect development, or premature decay of the neurons, causing idiocy, imbecility, and dementia. The neuron, like other cells, nourishes itself and is not nourished; and it depends for its development, life, and functional activity upon a suitable environment. It must also possess an inherent vital energy, by which it can assimilate and store up nutrient material, which may be regarded as latent energy, to be converted into nerve-force as required. A constant constructive and destructive bio-chemical process occurs in the nervous elements, and in a healthy nervous system the *balance of reserve* is high. The sense of fatigue is the natural indication for sleep and repose by which nervous energy may be recuperated. In the neuropathic and psychopathic individual it may be conceived that in some portions of the nervous system, especially the brain, there may exist communities, systems, or groups of neurons, with an *inherited low power* of storage of energy, rapidly becoming exhausted, and especially liable, therefore, to depression of function, the manifestations of which are hysterical paralyses, anaesthesias, katatonia, catalepsy, trance, and melancholia; or the bio-chemical substance, which represents this store of reserve, may possess an inherent chemical instability, and readily fulminate when an appropriate stimulus occurs, constituting thereby a place of diminished resistance in the nervous system. A general or localised bio-chemical instability of the nervous system may be followed by local or general discharge, with excitement and psycho-motor restlessness; these conditions, however, may be the result of lack of inhibition or of the highest control, whereby motor centres discharge more easily; uncontrolled ideation leads to rapid succession of thoughts by association and consequent impulses which find

expression in anti-social acts, whereby such persons often become dangerous to themselves and others. Lastly, there may be functional disturbance of the harmonious inter-relations of the motor neurons with failure of co-ordination, for example, Huntington's chorea.

The external causes producing morbid changes in the nervous elements depend upon (A) abnormal conditions of the blood and lymph, by which the neurons are poisoned, and their metabolism affected; (B) excess or deficiency of normal excitation, or the existence of abnormal excitation.

A. *Abnormal Conditions of the Blood and Lymph.*—The immediate environment of all the cellular elements of the body is lymph. In the central nervous system a special form of lymph, the cerebrospinal fluid, is secreted by the choroid plexuses (*vide* p. 266). The lymph serves as the medium of exchange between the blood and the tissues; and the essential causes of change in the environment of a nerve-cell are alterations in the quality and quantity of the blood-supply.

(1) Quantity of the Blood-Supply.—A frequent cause of disease of the nervous system is a failure of the blood-supply to some portion of the brain (*vide* pp. 214-219). A sudden failure of the heart's action causes a temporary loss of consciousness; and a generalised affection of the arteries, as in syphilitic arteritis, may, without thrombosis, produce disturbances of consciousness, semi-coma, drowsiness, and somnolent conditions as a result of insufficient blood-supply.

(2) Quality of the Blood-Supply.—Insufficiency of oxygen, due to anaemia, leads to functional depression, lassitude, fatigue, and mental exhaustion. Impoverishment of the blood in women, due to frequent pregnancies and excessive lactation, causes neuralgia, nervous exhaustion, and, in the neuropathic individual, hysteria, neurasthenia, melancholia, and mania. Probably there is an alteration in the composition of the blood in the nature of an auto-intoxication or possibly a "subminimal" deficiency. But the most striking examples of the effect of absence or "subminimal" deficiency of a normal constituent of the blood upon the development and functions of the nervous system are afforded by cretinous idiots, whose brains are arrested in development in consequence of the absence of the thyroid gland. Myxoedema in the later stages is attended by slowness of thought and speech, indicating that the nervous elements are unable to act normally owing to the absence of the internal secretion of the thyroid gland from the blood. This is proved by the disappearance of the nervous phenomena of myxoedema on compensating the deficiency by administration of the gland by the mouth.

(a) Excess of Normal Constituents in the Blood.—Carbonic acid and nitrogenous waste-products may be given as examples of normal constituents which, if in excess, induce symptoms of disease. Again, in Graves' disease, nervous phenomena in the form of palpitation, fine tremors, and mental excitement may be ascribed to excess of thyroid secretion escaping into the blood.

(b) The presence in the blood of abnormal constituents is the most

important extrinsic cause of nervous disease, and we may consider the subject under the following headings:—(i.) Poisons produced within the body by perverted functions of the organs or tissues (auto-intoxication), or by the action of micro-organisms upon the living fluids in the tissues of the body; (ii.) poisons introduced into the body from without.

(i.) Poisons produced within the Body.—The best examples of auto-intoxication are afforded by uraemia, the nervous manifestations of which are headache, drowsiness or coma, epileptiform convulsions, and sometimes symptoms of polyneuritis; excess of uric acid in the blood which is associated with high arterial blood-pressure, headache, and nervous irritability; diabetes (a result of imperfect metabolism) may cause multiple neuritis and coma, the latter being often heralded by acetonaemia, which may be regarded as evidence of a form of auto-intoxication, in which  $\beta$ -oxybutyric acid in the blood saturates the sodium salts and interferes with the normal tissue-respiration of the neurons; cholaemia, resulting from obstructive jaundice, may be attended by stupor and psychical depression. Again, the rapidly fatal results attending acute yellow atrophy of the liver, the profound changes in the urine and the blood, the jaundice accompanied by the nervous phenomena of delirium, motor irritation, delusions, stupor, and coma demonstrate the important part the liver plays in maintaining the normal quality of the blood. In pernicious and other grave anaemias, degenerative changes in the spinal cord, of the nature of a combined sclerosis, are frequently found, and are probably not so much due to the deficiency of red corpuscles as to some toxic substance arising from imperfect metabolism or microbic infection (*vide* Art. "Subacute Combined Degeneration").

We do not know the precise nature of the rheumatic virus, although it is probably microbic in origin, but we do know that it is especially liable to be followed by, or associated with, hyperpyrexia and chorea, indicating in the latter condition the action of the poison upon the cells of the cerebral cortex.

Examples of poisons due to micro-organisms occur in many infective diseases, such as enteric and typhus fevers, small-pox, scarlet fever, measles, influenza, pneumonia, septicaemia, and tuberculosis. Delirium, which frequently complicates these diseases, may be due to the high fever, or to the poison, or to both combined. In severe cases, stupor and coma may occur, and it has been shown that, in this extreme stage, the nerve-cells of the cerebral cortex, and also of the spinal cord, undergo an acute morbid bio-chemical change (*vide* p. 221). These particular poisons do not exert a selective action upon any special part of the nervous system, but many cases of neurasthenia, insanity, neurosis, and neuritis date their onset from an acute specific fever. Experiments by Homén, and by Orr and Rows, indicate that microbic toxins may pass up the lymphatics of nerves, and by the posterior roots gain entrance to the spinal cord and cause degeneration in the posterior columns.

In cerebrospinal meningitis, pneumococcic meningitis, "posterior-basis" meningitis, tuberculous meningitis, acute delirious mania, and leprosy



neuritis the inflammation of the enclosing and supporting tissues is due to the growth therein of the specific organism, and it may be presumed that syphilitic affections of the nervous system are due to the specific micro-organism, *Treponema pallidum*, attacking its enclosing, supporting, and vascular tissues. The characteristic chronic meningo-encephalitis of sleeping sickness is due to the invasion of the subarachnoid space by the *Trypanosoma gambiense*, for in all cases of sleeping sickness this organism is found in the cerebrospinal fluid.

Some Poisons have a Selective Influence upon some Part of the Nervous System.—The syphilitic poison is the most important factor in the production of two progressive degenerations of the nervous system, one affecting especially the afferent conducting tracts of the spinal cord, namely, tabes; the other attacking especially the frontal and central convolutions of the cerebral hemispheres, namely, general paralysis of the insane. A striking illustration of the selective action of the syphilitic poison is that the sign known as the Argyll Robertson pupil is confined to persons affected with acquired or inherited syphilis; seeing that this is the most common objective phenomenon in the two diseases mentioned, it strengthens the presumption, based on experience, that the syphilitic poison is the cause of these diseases. These diseases are often termed metasyphilitic or parasyphilitic (Fournier), and are degenerative processes, the result of an impaired vitality of the neurons causing premature decay and atrophy. Again, syphilis, when it attacks the supporting, enclosing, and nutrient vascular mesoblastic tissues, shews a predilection for structures about the base of the brain; thus, paralysis of the third nerve is almost pathognomonic of this disease. In rabies, although the whole nervous system is charged with the poison, the medulla oblongata is, as shewn by the symptoms, especially affected. Moreover, whether we regard the “Negri bodies” constantly found in rabies as a specific protozoon undergoing its life-cycle in the cells of the nervous system, or look upon these bodies as endocellular degenerative products caused by the specific virus of rabies, it is nevertheless true that the cells in the hippocampal region of the brain and the medulla never fail to shew these bodies in a case of rabies (*vide* Plate IV. Fig. 1). Seeing that the saliva is the infective agent, it is remarkable that the part of the brain presiding over taste and smell should be the seat of special affection in the nervous system. Again, in tetanus the bacilli elaborate a virulent poison which affects particular groups of neurons. The fact that “lock-jaw” nearly always occurs first, shews that the poison selects the motor nucleus of the fifth nerve. Further, it has been shewn experimentally that tetanus-toxin, if mixed with an emulsion of nervous matter before injection into an animal, loses its toxicity, thus proving its affinity for nervous matter, as well as a power of absorption of the poison possessed by some chemical substance in the nervous matter. Another example is offered by diphtheria; a neurotoxin is produced by the local action of the bacilli (*vide* Vol. I. p. 992), the effects of which are shewn by paralysis of the soft palate and of the muscle of accommodation, weakness and inco-ordination of the limbs



which may amount to paralysis, absence of knee-jerks, and often cutaneous anaesthesia, and by the not infrequent fatal termination from cardiac or respiratory paralysis.

(ii.) Poisons introduced into the Body.—The most widespread and potent cause of nervous and mental disease is the abuse of alcoholic stimulants. To people with unstable nervous systems a small quantity of alcohol acts as a poison. Beyond question neuropathic and psychopathic degenerates, criminals, lunatics, and imbeciles under the influence of alcohol, even in small quantities, become actively anti-social, thus leading to their detention in reformatories, prisons, asylums, and infirmaries. Still more obvious is it that all persons with a *locus minoris resistentiae* of the nervous system, whether inherited or acquired, either by injury or disease, are unable to withstand the effects of alcoholism. Chronic alcoholism is frequently associated with acute delirium and fine tremors, and generally with visual hallucinations of a terrifying nature, indicating acute toxic influence on the brain. This form of alcoholic poisoning is much commoner in men than in women, and it is remarkable how a severe illness, such as pneumonia, will bring out delirium tremens in a drunkard. Alcohol acts especially upon the higher centres of the brain, and a drunken man may exhibit "the abstract and brief chronicle of insanity, going through its successive phases in a short period of time" (Maudsley). The functions of the brain are stripped off successively in an inverse order to their development, namely, moral control and responsibility, deliberation and judgment, attention and concentration, memory and receptivity.

The ultimate effect on the nervous system of chronic alcoholism is dementia, a very characteristic manifestation of the mental degradation being absence of knowledge of time and place, personal illusions, mental confusion, and confabulation; and especially characteristic is loss of memory for recent events, which indicates a failure of receptivity and of the formation of memory pictures in the higher centres. Besides the mental symptoms of alcoholic poisoning there are frequently sensory disturbances and motor paralysis due to polyneuritis affecting especially the lower limbs; but the upper limbs, and even the heart and respiratory muscles, may be affected in severe cases. The improvement which generally occurs when total abstinence is enforced shews that the poison has damaged, but not destroyed, the nervous elements. This alcoholic dementia, termed Korsakow's psychosis, is much commoner in women than in men, and, according to my experience, is not solely due to alcohol; for in the majority of cases there is an accompanying intoxication of microbic origin. Married women who have had miscarriages and abortions, or have had salpingitis, endometritis, or parametritis, are especially liable to suffer. The frequency with which delusions of a child being in the bed occur may have some relation thereto.

Lead is peculiar in selecting the nerve-supply of the extensor muscles of the wrist and fingers, so that dropped wrist is almost characteristic of this form of toxic neuritis. Lead also produces a chronic inflammation

of the cerebral cortex (encephalitis saturnina), which gives rise to a complex of symptoms, namely, dementia, loss of memory, weakened intellect, hallucinations of sight and hearing, mental exaltation or depression, tremors, paresis, and epileptiform seizures. Arsenic has a special selective influence upon the peripheral nerves, causing polyneuritis, generally affecting all four limbs; sometimes severe psychological troubles and, in rare cases, epilepsy occur. Workmen in india-rubber factories may, as the result of inhaling the fumes of bisulphide of carbon, suffer with severe mental symptoms and polyneuritis. Carbon monoxide poisoning has always been common in countries where charcoal braziers are used; it is a cause of death in mines and blast-furnaces and of suicide or accidental death. CO-poisoning is not infrequent in England now, owing to the large proportion contained in illuminating gas. I have fully discussed this subject elsewhere (27). The immediate nervous symptoms are due to anoxaemia, but these are more or less temporary; permanent lesions from thrombosis and haemorrhages may occur, and may with other complications prove fatal, but if the patient recovers he may be permanently affected with dementia and signs of disseminated sclerosis, for example, scanning speech and intention-tremor. The immediate symptoms of CO-poisoning are variable (*vide* Vol. II. Part I. 1032). In addition to alcohol, some poisons act on the nervous system when introduced into the body as the result of a habit, namely, ether, cocaine, opium, morphia, hashish, and tobacco. "Such is the power of habit that, although doing certain things affords us no pleasure, we should be wretched if we did them not" (Sydney Smith). It is of interest to note that absinthe causes epileptic fits when taken for some time, and if intravenously injected into an animal produces epilepsy (*vide* Plate IV. Fig. 3).

*Beriberi*, a polyneuritis endemic in the East, is by most authorities believed to be due to the continued consumption of unsound mouldy rice. *Pellagra* is an affection of the skin associated with degenerative changes in the brain and spinal cord. The people so affected exhibit a fatuous melancholy, suicidal impulses, and sometimes mania. It is supposed that this disease is due to unsound mouldy maize. *Ergotism* is a disease due to consumption of bread made of rye which has been attacked by the ergot fungus. The poison thus introduced produces progressive degenerative changes in the brain and spinal cord. *Botulism*, due to eating decayed meat and fish infected with *Bacillus botulinus*, is a complex of symptoms, in which paralysis of the ocular muscles is an important feature (*vide* Vol. II. Part I. p. 860).

B. *Deficiency or Excess of Normal Stimulation or Existence of Abnormal Stimulation*.—Structure and function are mutually reciprocal and interdependent. A structure which is not used will gradually lose its function, while its nutrition will also suffer, and in time atrophy may occur. Amputation of a limb in early life causes atrophy of the nervous structures which preside over the sensation and movement of the part. This is seen in both the grey and the white matter of the spinal cord of the same side. A function not used will gradually disappear, and become more

and more difficult to evoke. This is of importance in functional neuroses and psychoses, for example, hysterical paralysis and melancholia, because the longer mental or bodily function is left in abeyance, the more likely is the defect to become permanent. The converse is also true; the longer a perverted function exists the less likely is it to disappear. Thus, auditory hallucinations, a very important and frequent symptom in the insane, commence with indistinct noises; these are followed by voices, and eventually the voices are so distinct and real that the greater part of the patient's psychical existence is concentrated upon, and determined by, this abnormal stimulus from within. Thus is shewn the progressive strengthening and fixation of the perverted functions of the mind, and progressive weakening and dissolution of the normal functions.

Abnormal Stimulation from without.—(1) *Psychical Stimuli*.—Mental pain in the form of grief, worry, anxiety, fright and shock, violent emotions, whether pleasurable or painful, disappointed love, sexual excesses or perversions, and excessive brain-work frequently precede and determine, in persons with the insane or neuropathic taint, various forms (*a*) of psychoses, such as mania, melancholia, delusional insanity; (*b*) of neuroses, such as chorea, hysteria, epilepsy, hystero-epilepsy; (*c*) of organic disease of the brain, such as apoplexy, thrombosis, and general paralysis. The effect of stress in determining neuritis and degenerative processes in the central nervous system can often be observed in practice. The most striking examples of psycho-motor functional paralyses from stress are afforded by writers', pianoforte-players', violinists', and typists' cramp, and hammermen's palsy.

(2) *Physical Stimuli*.—Visceral reflex irritation may act as an exciting cause of neuroses and psychoses; thus, intestinal worms, teething, and indigestible food, severally or combined, often produce in infants and rickety children convulsions, spasms of the glottis, and tetany. Various functional and organic diseases of the female reproductive organs act as exciting causes in the production of hysteria, hystero-epilepsy, melancholia, and mania; moreover, paroxysmal attacks in these diseases are more liable to occur at the menstrual period or at the menopause. The irritation of a carious tooth may produce trigeminal neuralgia. Wax in the ear may occasion vertigo and tinnitus aurium, and errors of refraction may be the cause of attacks of migraine, and even excite epileptic fits in a person with an inherent epileptic tendency or the subject of epilepsy. Numerous other examples of peripheral disturbance could be mentioned as exciting causes of nervous affections, for example, irritation of the terminals of the vagus in almost any part of its widespread visceral distribution may lead to reflex vomiting. The characteristic pain of angina pectoris, which radiates down the inner side of the left arm, is explained by the origin of the cardiac branches of the sympathetic from the same segments of the spinal cord as the sensory branches of the ulnar nerve; consequently the pain is referred to the corresponding skin area supplied by this nerve. This is one example of a great number of *referred pains*.

Commotion of the brain and spinal cord, caused by the shock of



motor and railway accidents, blows, and falls, without producing concussion or injuries of the bony enclosing structures resulting in compression of the central system, is apt to produce traumatic neurasthenia. Examination of the nervous system in such cases does not reveal any obvious morphological change in the neural structures, and yet functionally they are altered; their bio-tonic equilibrium is affected, for the subject of traumatic neurasthenia is much more easily affected by poisons, and a quantity of alcohol which previously had little or no influence produces toxic effects.

**THE FUNCTIONS OF THE NEURON.**—**The Neuron; Excitable Cell and Conductor.**—Every neuron is an excitable cell; it is also a conductible cell, and a change excited at the receptive end is propagated through the whole neuron. The molecular change constituting a nervous impulse is never reversed, and always circulates in one direction. This has been termed by James “the law of forward direction.” The nervous impulse is immeasurably small in quantity, its duration at any one point of the neuron is brief, namely, one-thousandth of a second; it travels at the rate of about 30 metres per second, and the wave has a length of about 20 millimetres. In propagation along a chain of neurons the impulse is profoundly and variously modified; it may be modified in the ganglion-cell through which the conductible fibrils pass, or it may be at the synapse or junction of the terminal processes of one neuron with the processes of another. In normal physiological conditions a nerve-fibre is immune to fatigue. The centre, on the contrary, is easily fatigued by excessive functional activity. Had the cell-bodies of the neurons only trophic functions, and were the fibrils the special seat of reflex function, we should expect that the centre where the fibrils stand in direct connexion with the ganglion-cells would be much less easily fatigued than the peripheral nerves, but it is just the reverse; that the nerve-fibre does not undergo fatigue proves that there is some integrating substance or structure included in the reflex arc. This may be in the ganglion-cell itself, or it may be at the junction of the processes of one neuron with another, the synapse of Sherrington (*vide* Fig. 42).

**Reflex Action.**—All nervous actions are reflex actions, and we should therefore first inquire, what is understood by the term reflex action? It is brought about by a stimulus which may be defined as a change in the environment which acts on the organism as an exciting agent. The energy imparted to the organism by the stimulus is usually far less than the energy liberated by the organism itself. This excess of energy must be referred to energy generated in the organism itself. The conception of a reflex action then implies separate structures: (a) A receptor or initiating organ; (b) a conductor; (c) an effector. Every reflex is an integrative action, and no nervous action short of a reflex is a complete act of integration. A simple reflex is probably a purely abstract conception, because all parts of the nervous system are connected together.



It is, however, a convenient, if not a probable, fiction. In the simple reflex, receptor, conductor, and effector each plays its part, and Professor Sherrington's beautiful experiments shew that adaptation of the organism to its environment for the preservation of the individual and the species has evolved a perfect pre-organised automatic spinal reflex mechanism for each of which some particular biological stimulus is appropriate. The receptor by virtue of a special structure acquires a selective excitability, and plays a very important part in nervous reactions; for while providing increase of responsiveness to changes of environment, at the same time it limits its excitability to particular stimuli, which give rise to particular instinctive reactions, and thus tends to avoid confusion of reflex responses and inco-ordination.

But before considering further the linkage of the neurons in the production of simple and complex reflex actions, it is necessary to discuss the processes occurring in the neuron as a conductor and a generator of nervous energy. The characteristic differences between conduction in reflex arcs and nerve-trunks respectively are:—(i.) Retarded transmission. The central rate of conduction is fifteen times as slow as the rate in nerve-fibres. (ii.) The central resistance is such that, whilst considerable for a single nervous impulse, it is easily forced by a succession of impulses. (iii.) Instead of reversibility of direction of current, as in nerve-trunks, there is irreversibility. Professor Gotch and Sir V. Horsley shewed that there is a complete block to transmission from the afferent into the efferent neurons. (iv.) The susceptibility to fatigue shewn by the cell is in striking contrast to the comparative insusceptibility to fatigue of nerves. (v.) The central efferent discharge has a special periodic character. (vi.) The central efferent discharge may continue after the afferent nerve-impulses have apparently ceased. (vii.) Refractory period (*Bahnung*), inhibition, and shock exist in degrees unknown for nerve-trunks. (viii.) There is a much greater dependence on blood-supply and oxygen than is the case with the nerve-trunks. (ix.) There is a much greater susceptibility to various poisons, drugs, and anaesthetics than is the case with nerve-trunks. These remarkable differences are referable to the grey matter of the central nervous system, which consists of the neurons and a supporting framework of neuroglia; they cannot depend on the latter, which has nothing to do with conduction. It is hardly justifiable to suppose that conduction along nerve-fibres assumes in the grey matter characters different from those it possesses elsewhere, and there is evidence that the fibrils of the neurons in the dendrons, axons, and cells are continuous with the axons of the nerve-fibres outside, and I therefore agree with Professor Sherrington's conception that there is a surface of separation between neuron and neuron. He points out how the existence of such a surface could either physically or chemically explain the facts above related; he inclines to the physical explanation. Thus, the intercalation of a transverse surface of separation into the conductor must modify the conduction, and it would do so with the same results which

are known to differentiate reflex-arc conduction from nerve-trunk conduction. Moreover, we have seen, in discussing the neuron doctrine, that there is much evidence in favour of the view that the neurons are in contiguity, not continuity, by an immense number of fine terminal



FIG. 42.—Scheme of reflex action after Edinger, somewhat modified to indicate the synapse. S, sensory neuron, the terminal arborisation of its fibrils in the skin forms the receptor; its proximal fibrils terminate in the synapse *Sy*, where it is brought into direct relation with the fibrils of the dendritic processes of the motor neuron *M*<sup>1</sup>; it is also brought into relation with the dendritic fibrils of the association neuron A: this again is connected by the synapse *Sy* to the more or less remote motor neuron *M*<sup>2</sup>. Stimulation of the sensory receptor in the skin may give rise to the following results: excitation of *M*<sup>1</sup> with direct reflex contraction of the muscle attached to the skin excited; at the same time an inhibitory influence may pass to *M*<sup>2</sup> through the association neuron A if the biological stimulus necessitates a quicker reaction and the two muscles are antagonists. If, however, *M*<sup>2</sup> is remote and not antagonistic to *M*<sup>1</sup>, then, as in the case of the scratch reflex, a suitable biological stimulus of the sensory receptor may by the association neuron excite *M*<sup>2</sup> and cause reflex contraction of distant muscles. These association neurons are essential for all purposive protector reflexes where a particular group of motor neurons form the final common path to groups of muscles employed for different purposes.

points, which may possess amoeboid properties, the terminal points of the fibrils of one neuron being attracted to, or retracted from, the terminal points of another, according to the activity of its protoplasm, excited by stimulus. This would be a physical explanation, and it may be further postulated that the passage of stimulus through the fibrils of the

cell, where the store of latent-energy substance is deposited, converts the latent energy into kinetic, and this excites the delicate fibrillar tentacles to amoeboid movements, which, after a shorter or longer delay, according to the effect of the bio-chemical stimulus, lead to the formation of innumerable ultra-microscopic protoplasmic bridges connecting the terminal fibrillae of one neuron with those of another. The amoeboid movement would only take place in the line which it had always followed, namely, from afferent to efferent neuron, or afferent to association neuron, or association to efferent neuron (*vide* Fig. 42). A bio-chemical explanation of the facts is not so clear, but it has been supposed by Scott that the chromophil substance of the ganglion-cells is a store of organic material representing latent energy, analogous to the pro-ferment of the secretory glands, and that in the presence of oxygen and a stimulus it is continually transformed into a substance capable of liberating active energy at the terminal points of the neuron, and, discharging, excites the fibrillar terminals of the next neuron so soon as sufficient energy has developed. This conception would also account for delay and summation of stimulus. The convenient term of "synapse" has been applied to this alterable conductor, upon which so much of the functions of the central nervous system depends, and the study of which will probably prove to be the key to unlock the mysterious problems of the neuroses, psychoses, and so-called functional diseases of the nervous system. The obvious advantage of this *alterable conductor* over the fibrillar *continuum* found in the lower invertebrates is that the same motor neurons and muscles are thereby capable of an infinite number of actions; for, as Professor Sherrington has shewn experimentally, the same groups of spinal motor neurons are the final common path of a number of automatic instinctive actions necessary for the preservation of the individual and the species (*vide* pp. 244-249). The synapse shews a variability of conductivity under different conditions; there may be a resistance to the passage of impulses—the refractory phase—the importance of which in purposive reflex mechanisms cannot be overestimated. It may be defined as the period of time during which stimuli adequate to produce contraction cease to pass. A beautiful example of this refractory phase is afforded by the rhythmical contraction and relaxation of the swimming-bell of the medusa and the beating of the heart. It is associated, therefore, with some altered condition of the nervous or contractile substance. It is also seen in the scratch reflex (*vide* p. 245).

**Metabolism of the Neuron in relation to Function.**—Every healthy living cell nourishes itself, and is not nourished, and possesses a metabolic equilibrium. Now it has been shewn that the neuron is a very complex highly-differentiated cell, obeying, however, the same laws of nutrition and of repair and waste as other cells of the body. A neuron, however, differs from the other cells in the body in being perpetual. All the neurons are present at birth, and they grow and develop especially by an increase of the fine branching terminal fibrils which form the apparently inextricable network of the grey matter of the central nervous system.

Every neuron has a specific energy of its own, and its functional capacity and durability will depend upon three factors: (i.) The inherent vital energy to maintain bio-tonic equilibrium; (ii.) The condition of the circumambient medium which provides the necessary chemical substances for functional activity and repair of waste; (iii.) A capacity of the neuron for storage of energy, whereby it is enabled to meet stress under conditions in which immediate repair of waste is rendered difficult or impossible. Bio-tonic equilibrium when disturbed, provided it has not overstepped physiological boundaries, is sooner or later restored by rest, which permits a sufficiency in the processes of assimilation to take place.

The phenomena of fatigue of the ganglion-cells has been studied by Hodge, Mann, Pick, Lugaro, Guerrini, Gordon Holmes, and others. All who have studied this subject have observed similar changes in the Nissl bodies. Fatigued ganglion-cells shew a diminution of the basophil-staining substance and changes in the nucleus. No alterations have been detected in the nerve-fibres. It may therefore be inferred that this substance contained in the ganglion-cells and protoplasmic processes is used up by excessive functional activity. It does not necessarily follow that the active chemical processes connected with nervous action occur in the cell; it is possible that the bio-chemical changes incidental to nervous activity take place at the terminal arborisations of the nerve-cell within the grey matter.

**Experiments relating to the Bio-Chemical Processes occurring in the Ganglion-Cells during Work.**—Concerning the constructive metabolism taking place in the ganglion-cell during rest we know very little. The phenomena of fatigue have been studied by Verworn and his pupils in the frog. He has produced an artificial circulation of oxygen-free salt solution in the animal and afterwards injected strychnine; the slightest peripheral stimulation then produced a maximum amount of work. Clearly, then, the strychnine allowed a store of oxygen-containing substance to be drawn upon, for there was none in the circulating fluid. If, however, the artificial circulation ceased and the oxygen-free fluid was allowed to stagnate in the capillaries, then the tetanic spasms became weaker and weaker, and finally no response was obtained. On restoring the artificial circulation, the irritability of the centres was restored after a few minutes, and the tetanic spasms returned; in time, however, they became weaker and occurred at longer intervals, and then ceased altogether. The spinal centres were therefore capable of discharging without receiving oxygen or nutritive material; it must be presumed that the spinal motor neurons possessed a store of latent energy which, under the influence of the strychnine and the stimulus, could be converted into kinetic energy independently of oxygen in the circulating blood. But to maintain a continuity of action, oxygen is necessary, and when all reflex response is lost, the circulation of an oxygenated medium suffices to restore the excitability. H. von Baeyer was able in certain cases, with a sufficient supply of oxygenated fluid, but without any



nutritive material in the fluid, to obtain reactions in the frog for ten to twelve hours, and Baglioni maintained the isolated spinal cord of the frog irritable for forty-eight hours. From these researches the following conclusions may be drawn. Two processes occur side by side during excessive activity of the ganglion-cells:—(a) A loss of function from the accumulation of the products of destructive metabolism, which may be termed *fatigue paralysis*; and (b) a loss of function owing to failure of repair of waste, which may be termed *exhaustion paralysis*. This condition of exhaustion may result from failure of its oxygen-storage, or, in exceptional experimental conditions, from failure of organic material. The ganglion-cell contains reserve stores of oxygen and of organic material. The former are much more readily exhausted than the latter. When a



FIG. 43.—Cells of the medulla oblongata shewing extreme chromatolysis. The specimen was obtained from the brain of a man who died seven hours after receiving a charge of electricity of 20,000 volts. This case was described by Dr. Schuster and myself. All the cells of the central nervous system shewed a similar change. The intracellular and intranuclear networks are apparent, and practically all the chromophil substance has disappeared. The change may have been due to the direct effect of the current upon the osmotic membrane of the cells, as there was considerable haemolysis of blood-corpuscles. Magnification, 500; staining, polychrome methylene blue and eosin.

nervous centre is exhausted by excessive work, it is on account of the using up of this reserve oxygen-substance, and the neuron is, as it were, asphyxiated, for the store of organic material in the neuron cannot be exhausted under physiological conditions; only experimentally can it be shewn that this substance can be exhausted by excessive work without a renewal of supply. When excessive work has to be performed by a frog for a long time under the artificial condition of a circulation of oxygenated salt solution, the whole of the store of carbon-containing energy-substance is oxidised out of the ganglion-cells, and Dr. Gordon Holmes has shewn that the spinal motor cells of such a frog, stained appropriately, no longer contain any Nissl granules. It may therefore be inferred that this

substance which forms the Nissl granules is used up by work, as the fatigue experiments already referred to on page 210 indicated. The most marked chromatolytic changes I have seen were those shewn in Fig. 43.

The researches of von Baeyer and Winterstein have given important results concerning the mode of storage of the reserve oxygen. They have shewn that the ganglion-cells in the frog are able to assimilate larger quantities of oxygen at lower temperatures, because, with a rise of temperature, larger quantities of oxygen are used up, therefore the addition of oxygen from without cannot, at a higher temperature than normal, keep pace with that which is used up within the neurons. At a temperature of  $33^{\circ}$ - $35^{\circ}$ C. paralysis occurs in the frog owing to failure of oxygen—that is, a condition of asphyxia-exhaustion occurs which can only be remedied by a renewal of the oxygen at a lower temperature. By analogy with other cells, we should judge that the oxygen is diffused throughout the whole nerve-cell in a state of chemical combination. The refractory stage of the nerve-cells, discovered by Broca and Richet, which occurs after a discharge associated with destructive metabolism, depends, according to Verworn, on oxygen-exhaustion, and, therefore, upon conditions relating to the storage of the oxygen-holding substance.

It has been shewn experimentally that with progressive exhaustion of the oxygen store in the neuron, the refractory stage lasts longer and longer with each discharge of impulses, and that the interval of time is dependent upon the time required for a sufficient number of oxygen molecules to be provided at the necessary points to be excited for a new discharge. The refractory stage in the frog's spinal cord can be prolonged by a withdrawal of oxygen from one-twelfth of a second to over one minute. The refractory stage caused by exhaustion of the oxygen-substance is one of the important conditions necessary for *rhythmical activity* which may be observed in many centres, and it affords an explanation of the occurrence of tonic excitation presenting an intermittency. After each discharge, which has set up a dissimilating exciting impulse in the ganglion-cell, by virtue of an internal self-regulating mechanism, there is a return to the original condition of excitability. This return depends, in the first place, upon the removal of the products of dissimulation, among which we may safely reckon carbon dioxide, and, secondly, upon the replenishment of oxygen-substance.

The loss of function of the neuron may then arise from disturbances affecting different factors entering into its metabolism. We have already discussed those concerned in the phenomena of exhaustion of fatigue. The paralysing of function in the neuron, which arises as a result of the action of narcotics, belongs to the phenomena of fatigue, and the researches of Meyer and Overton shew that the effects of a narcotic depend upon the greatness of the partial coefficient between the solubility of the drug in plasma-lipoids and in water. The narcotic, in order to produce an effect upon the metabolic changes incidental to the functions of the cell, must be able to penetrate the plasma-lipoid membrane; and to effect this, and to modify the bio-chemical changes in the cell protoplasm

within, it must be soluble in certain proportions both in plasma-lipoids and water. Still, this does not explain the mechanism by which narcotics paralyse the action of the ganglion-cells. But the researches of Winterstein have led to the conclusion that narcotics paralyse the oxygen-intake of ganglion-cells; for when these cells have been exhausted of oxygen and then narcotised, they are unable to take it up even when it is supplied in abundance, and the experiments of Winterstein tend to prove that narcotics hinder the transference of the molecules of oxygen from the oxygen-store to the place where oxidation-processes occur. The block to the use of the stored oxygen causes a functional paralysis of the neuron by a process of asphyxia. When the temperature of the body rises above the normal there is first an excitation of the neuron, then exhaustion; the exhaustion is the result of the oxygen being used up faster than it can be replaced and stored, and the neuron ceases its functional activity; it is not, however, destroyed unless the temperature rises to such a degree as to produce a heat-coagulation of the neuroglobulin. This change occurs in hyperpyrexia (*vide* p. 234). Low temperatures diminish dissimilating processes, and therefore there is diminished functional activity of the neuron.

**Processes occurring in the Nerve-Fibres.**—The nerve-fibre, in the light of the neuron doctrine, cannot be considered apart from the nerve-cell and its processes, for its essential axial core is a process of the cell consisting of neuro-fibrils with a very small amount of interfibrillar substance. It has been already remarked that the nerve-fibre is comparatively immune to fatigue, and the question which naturally arises is this: Do the metabolic processes which occur in the ganglion-cells also take place in the nerve-fibres?—in other words, does the production of excitation in the nerve-fibre as well as in the ganglion-cell depend upon metabolic changes? A nervous impulse was formerly believed to be a physical process, because a nerve-fibre cannot be brought into a condition of fatigue by the transmission of impulses; in fact, it was thought that the nerve-fibres behaved like the insulated wires of a telegraph cable, except for the fact that the rate of transmission was only 30 metres per second. Innumerable publications have appeared upon the electrical properties of nerves without affording much advance in our knowledge of the vital processes which occur in nerve-fibres during the conduction of a stimulus; and although the production of electrical variations in nerve has served as a useful indicator for the presence, continuance, and the intensity of processes occurring in nerves, it has, according to Verworn, taught us little concerning the nature of these processes. Yet it is probable that electrical currents do play a part in the changes which take place in its living substance; but we do not know how or what part they play. During the last few years valuable experiments have been performed, throwing some light upon the processes occurring in nerve-fibres during the transmission of an impulse. Von Baeyer has shewn that a tetanised nerve in an atmosphere of pure nitrogen loses its irritability and conductivity. Moreover, he has found that a complete

return to the normal may be brought about by admission of oxygen. Probably the sheath has the power of storing oxygen, or of replacing it as fast as it is used up; but whatever may be the explanation of the oxygen storage and replacement, this experiment proves that oxygen is stored and used up, and that metabolic processes take place in this part of the neuron similar to those in the nerve-cell of which it is a process. Thörner, moreover, has shewn that by continuous tetanic excitation of the nerve in air a stage of commencing fatigue is easily brought about; for if a nerve during this stage of commencing fatigue be placed in nitrogen, it passes more rapidly into paralytic fatigue than a nerve not previously tetanised. It may therefore be concluded that it is not correct to say that nerve is absolutely immune to fatigue.

We are indebted to Verworn and his pupils for the foregoing experiments on the neuron in the frog under various conditions of alteration of the circumambient medium. They are of great interest, because they confirm and accord with those which have been performed in the higher warm-blooded animals, as the following experiments shew. It has been abundantly proved that whenever a healthy neuro-muscular tissue is rendered anaemic, a stage of hyper-excitability of function precedes that of paralysis. It has, moreover, been determined that the onset of these two stages may be delayed by cooling the tissues. This we have seen in cold-blooded animals; in the frog, for example, it has been shewn to be due to the utilisation of the store of reserve oxygen, and that cold delays this process of transference of latent into active energy. Deoxygenation of the blood, as in asphyxia, provokes exactly the same sequence of events.

**Blood-Supply and Nervous Action.**—Dr. Hughlings Jackson, in 1864 and since, has pointed out that embolism of cortical arteries frequently causes convulsions, and Schiff shewed that unilateral convulsions can occasionally be obtained by unilateral compression of the carotid in man. Dr. L. Hill, practising on himself, states that the cortical discharge is unaccompanied by consciousness of the movement; he was aware of clonic spasms by the arm striking the chair on which it rested. He considers that instability of the cortical cells rather than failure of freedom of circulation in the circle of Willis is the cause. In the light of Verworn's experiments this clonic spasm may be explained by intermissions of the tonic equilibrium and discharge to the lower centres from the Betz-cells, owing to periodic rhythmical refractory-phase conditions arising from insufficiency of oxygen. Complete anaemia of the brain abolishes cortical excitability in about one minute. Dr. L. Hill has ligatured both carotid arteries and both vertebral arteries in dogs, and then he has injected Ehrlich's vital methylene blue. When the cortex was exposed, the blue tint was distinctly visible. This blue tint may be due to liberation of oxygen from the reserve store in the ganglion-cells. Stimulation of the fore-limb area by a faradic current just perceptible to the tongue gave a well-marked reaction followed by a fit; and it was observed that the cortex became pale, indicating that the oxygen which



had been liberated in a free state had all been used up. Fifteen minutes later the blue colour returned, and the same experiment was repeated with the same results. It is quite possible that the cerebrospinal fluid contains enough oxygen to produce this effect of restoration of function by restoration of oxygen; or it may be that time is required for the conversion and transference of latent into nascent oxygen. When the cortex is excited and no pallor occurs, no motor action results. The ganglion-cells are only capable of discharging under the influence of stimulus when a sufficiency of latent oxygen has been converted into nascent oxygen, as revealed by the return of the blue colour.

Cerebral anaemia in man rapidly produces a loss of consciousness, and it is probable that the higher cortical neurons do not possess so large a store of oxygen reserve as the subcortical neurons. Still, ligation of all four arteries in animals, dogs and cats, and of both carotids and one vertebral in monkeys, produces only temporary functional defects. Dr. L. Hill performed this operation on animals. He found that the animal, on recovering from the anaesthetic, exhibited in varying degrees, and as a rule for a few days, at the most a week, symptoms pointing to loss of function of the cortical grey matter. The animal was in a condition like Goltz's dog with its cortex destroyed. It wandered about with its legs splayed out, taking no notice of a flame, tobacco-smoke blown into its nostrils, or of its food, although it would eat food when placed in its mouth. A cat placed near it did not excite attention, it would not answer to a call, sensory stimuli did not awaken in its cortex a psychical response. All these symptoms passed off more or less rapidly, and no difference could be detected between its behaviour and that of a normal dog. Examination shewed that the collateral circulation had been restored by the anterior and posterior spinal arteries becoming as large as the vertebrales. In some instances a more profound cortical anaemia was produced by ligation of two carotids, one vertebral, and one subclavian at a point before the vertebral is given off, thus leaving practically only one superior intercostal to carry on the circulation. In such cases the anaemia was more profound, and sometimes caused death within twenty-four hours by the insufficiency of circulation in the medulla and choroid plexuses; in animals which survived, dementia was more profound and more persistent, and the histological changes observed in the cortex came on sooner and were more pronounced. Cats and monkeys, as a rule, died within twenty-four hours after ligation of the four arteries. Death followed convulsions preceded by coma. The histological changes observed in such cases of complete anaemia were quite different to those observed in severe but partial anaemia (*vide* Vol. I. Plate VII. Figs. 2, 3). It was found that faradic excitation of the cerebral cortex of animals with severe, but not absolutely complete, anoxaemia was followed by characteristic motor responses; but there was a tendency to spread, and, even with a moderate current, for epilepsy to occur. The motor path was open from the cortex, and capable of conducting stimuli, and this explains why no paresis followed the ligation of four arteries provided that the

animals recovered by restoration of the collateral circulation. Examination of the motor cortex of the brain at varying dates after the operation shewed, by the Nissl method, swelling of all the cortical cells. The nucleus was large, pale, and clear, sometimes occupying an eccentric position; the Nissl substance was diminished, and a fine chromophil dust incrusting the fibrils, giving it the form of basophil-coloured threads. The large Betz-cells, however, shewed Nissl granules in fair abundance (*vide* Vol. I. Plate VII. Figs. 2, 3). The swelling of the cell, the alterations in the basophil Nissl substance, and the nuclear changes are much more pronounced in the smaller cells of the cerebral cortex, especially the small and medium-sized pyramids. Numbers of these may be found with crumbling edges, ruptured cell-walls, and extruded nuclei; only a few of the large pyramidal cells are thus affected. These remarks apply to the monkeys' brains in which a severe temporary anaemia had been produced. Examination of the spinal cord by the Marchi method, the animal being killed ten days or more after operation, revealed only a comparatively few degenerated fibres in the crossed pyramidal tracts. This proves that such marked changes as those shewn (changes, indeed, which, if they were not controlled by restoration of function and absence of evidence of degeneration of their axons, might be termed degenerative) are really only functional. Moreover, sections stained for fibrils by the Cajal method shew the integrity of the essential fibrillar conducting substance. The fibrils of the large psycho-motor neurons of three animals which were killed twenty-four hours after ligation of four arteries were examined by this method, and the fibrillae of the dendrites could be traced up to the superficial layer of the cortex in the brains of the animals (two cats and a dog). This explains how it is that cortical excitation by faradisation evokes movements readily in these anaemic brains of temporarily demented animals. Powerful stimuli will sometimes arouse a purposeful reflex response; for example, a cat that had all four arteries tied, and took no notice of ordinary sensory stimuli, on the approach of a dog was aroused from its prone position, and in an inco-ordinate manner attempted to scratch the animal. Likewise a monkey, four days after ligation of three arteries, was in an absolutely demented condition, with rigidity of all its limbs, yet on the approach of a cat was roused to attempt flight. These instances shewed that an instinctive biological stimulus has a most powerful effect upon the subcortical centres, and may operate in producing a purposive action, when the animal is deprived of its higher cortical functions. Subsequent examination of this animal's brain revealed the most profound bio-chemical changes in the cells of its cortex, corresponding to those produced by complete cortical anaemia.

The importance of the carotid supply in the monkey, and therefore in man, was shewn by Sir V. Horsley and Mr. Spencer. They compressed the carotid artery in the monkey. No change was observed in the pulsation of the anterior and posterior cerebral arteries; on the other hand, the pulsation ceased to be visible in the middle cerebral artery. Now

this artery is in a direct line with the axis of the carotid as it enters the circle of Willis. When the excitable motor cortex was stimulated before compression, a response was obtained with a much weaker current than during compression; and after compression the current required to evoke a response was stronger than before compression.

If the blood-supply<sup>1</sup> to the brain of a monkey is so completely cut off—by clamping both carotids and ligating the vertebrals—as to render the motor area inexcitable, the removal of a clamp on one carotid artery renders the corresponding hemisphere excitable, and in about one minute the motor response can be obtained. On again clamping the artery the excitability diminishes, and in about one minute no motor response can be elicited, even on very strong stimulation. Again, in some experiments which I performed with Prof. Sherrington we found that compression of the spinal cord in the mid-dorsal region, so as to indent the spinal cord, did not interfere with the transmission of impulses by the pyramidal fibres; for on faradic excitation of the motor area in the monkey, movements were as easily evoked in the lower limbs as previously. If, however, very slight compression of the lumbo-sacral region were made so as to interfere with the circulation in the grey matter, then the strongest excitation in the leg area ceased to produce any movement after about one minute. On removing the pressure, so as to restore the circulation in the lumbo-sacral grey matter, the block to the passage of the stimulus was soon removed, and in one to two minutes a current of moderate strength gave a normal response. *This fact points to an oxidation process occurring at the terminals of the neurons of the motor path in the grey matter of the spinal cord; and proves that the metabolic changes incidental to functional activity occur where the vascular supply is most abundant.* This chemical change is the source of neural activity.

Do the neurons, either when excited by faradisation, or acted upon by convulsants in the absence of a sufficiency of oxygen, shew changes which might be interpreted as indicative of fatigue? Observation of sections, prepared by the Nissl method, of the two hemispheres of a cat's brain rendered almost completely anaemic by ligation of arterics, did not shew any recognisable difference in the appearance of the cortical cells of the two hemispheres, although one had not been excited at all, and the other had been faradised at intervals for two hours. But then, from what has been previously said, no response is obtainable unless oxygen is used up. Then, it may be asked, how it is that the cortex remains excitable when the oxygen is so obviously deficient as compared with the normal. The normal effect of excitation of the cortex is both excitatory and inhibitory on groups of correlative antagonistic muscles; and it is conceivable, nay, probable, that the reason a moderate, or even a weak current, even with a deficient supply of oxygen to the cortex, and therefore a proportional feeble chemical metabolic change, evokes a motor response is, that an excitatory impulse is obtained, and not being neutralised by inhibitory innervation currents, a much fuller cortical discharging impulse suffices (*vide* p. 250). Moreover, the main expenditure of chemical



energy in the cerebral cortex is concerned with inhibition, a function later acquired, and probably dependent upon the functions of cortical neurons of later ontogenetic and phylogenetic development (the layer of small, medium, and large-sized pyramidal cells situated above the layer of granules), which it has been observed are more affected histo-chemically by the ligation of the vessels (*vide* p. 216). These pyramidal cells are the neurons which subserve the functions of associative memory; in this layer are revived the memory-images of past experiences upon which judgment and volition depend. This layer of pyramidal cells I find increases in superficial extent and thickness in vertebrates as we rise in the zoological scale, until in man it forms the great bulk of the grey matter of the cerebral cortex. Moreover, Dr. J. S. Bolton, by a series of careful metric measurements, has shewn that this layer is especially wasted in dementia and deficient in amentia.

In fact, there is a parallelism between the loss or deficiency of mind and the decay or deficiency of the supragranular pyramidal layer. Moreover, in the brains of animals temporarily demented, these pyramidal cells are, as compared with the large Betz-cells, especially swollen and altered in their appearance; but probably another reason why there is no longer the possibility of reviving memory-images in these animals is the lack of oxygen at the synapses of the terminals of the sensory projection-system with these cortical association-neurons.

The fact that the two kinds of change observed in the cortex as a result of ligation of arteries in great measure resemble the changes observed in many toxæmic conditions supports the conclusion that toxins act upon the neural elements in such a way as first to excite them, and later to depress their functional activity, or to abolish the normal metabolism necessary for their functional activity. Animals that either died within twenty-four hours, or never recovered from the demented and parietic condition, presented changes in the cortex quite different to those that recovered. There was sometimes chromatolysis and a physical change due to altered osmotic conditions and absorption of cerebrospinal fluid causing a dropsical appearance of the cell, with swelling, eccentric position, and even extrusion of the nucleus. Sometimes, when there was thrombosis of the arteries, or when the secretion of the cerebrospinal fluid was prevented, causing thereby a lack of the ambient medium and complete anoxæmia, the cells were not swollen, but shrunken. The staining reaction was also different, shewing that an irrecoverable biochemical change had taken place. When the sections were stained with a double stain of methylene blue and safranin or when polychrome blue was used, the whole cell was stained uniformly pink or dull purple, and did not shew the brilliant differential coloration of the Nissl bodies and fibrillar substance as in the normal. This condition is somewhat similar to that in hyperpyrexia, and identical with the appearances described by Sarbó in the motor spinal neurons of the lumbo-sacral region after clamping the abdominal aorta. A monkey which was killed five days after ligation of both carotids and one vertebral, presented the most



destructive changes (Fig. 61). The ganglion-cells and all their processes were uniformly stained a dull purple; the perivascular spaces were greatly dilated, the vessels were empty, but there was little evidence of inflammatory reaction. Scattered through the protoplasm of the cells was a fine purple-stained dust; the apical processes of many of the pyramidal cells were destroyed or twisted like corkscrews; the dendritic processes were destroyed or swollen and irregular in form. Some ganglion-cells could be seen in a state of advanced necrobiosis with phagocytic cells sticking to them. Although the Nissl method shewed this profound change in all the cells of the cortex, yet the rapid Golgi method displayed numbers of pyramidal cells with gemmules on the dendrons and all the external appearances of a normal pyramidal cell. This animal was paretic and demented. I mention this point because it demonstrates the untrustworthiness of observations appertaining to mental states caused by pathological changes in the cortex, which are based solely on this excellent anatomical, but unreliable (Golgi) method when applied to the demonstration of cerebral lesions in toxic psychoses.

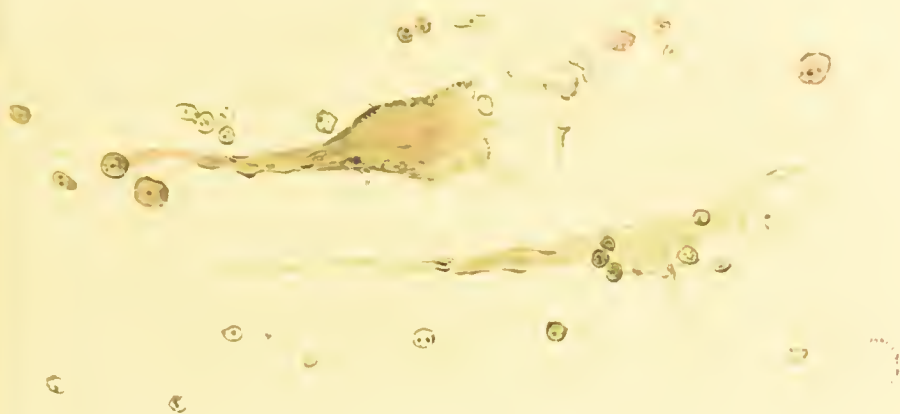
These results upon temporary and permanent dementia caused by temporary and complete anaemia of the cerebral cortex have the following important bearings upon the subject of the pathology of the nervous system. (1) Complete restoration of cortical function may occur provided that collateral circulation is re-established before bio-chemical changes of coagulation-necrosis occur. (2) The restoration of function in the transitory aphasias, word-blindness, word-deafness, monoplegias, hemiplegias, and disturbances of consciousness met with in syphilitic endarteritis cerebri, is explained by a temporary anaemia occasioned by occlusion of an artery without spreading thrombosis occurring. Collateral circulation restores the function. Also the extraordinary recovery from seizures of general paralysis suggests that some of the symptoms may be due to functional disturbance of the cortex brought about by circulatory derangements. A large number of the cortical cells in general paralysis shew acute changes due, no doubt, to vascular disturbances. Many exhibit the swollen dropsical condition of functional change, yet, as the dog's anaemic brain proves, these cells are capable of recovery; others shew an acute necrobiotic change, and are incapable of recovery. The cortical cells in a state of acute decay may be hyper-excitabile, and if the morbid process affects the motor area, as it so frequently does, then twitching of the muscles and clonic spasms may result, followed later by an increase of the paresis. (3) Carbon monoxide poisoning produces anoxaemia of the nervous system, and the symptoms vary in different individuals according to the amount inhaled and other conditions. The temporary effects are in some instances remarkable; a most valuable account of the effects of CO-poisoning is given by Sir Le Neve Foster and Dr. Haldane shewing that individuals exposed to the same mine-air are not affected in the same way. Thus, Sir Le Neve Foster states that the poison paralyzed him and dulled his feelings, but his reason did not leave him. Two other gentlemen, though not absolutely unconscious, did not

## PLATE II.

Fig. 1.—Section of the top of the ascending frontal convolution of the brain of a lad, aged eighteen, who died eight weeks after fracture of the spine causing a total transverse lesion of the spinal cord in the lower cervical region. Two Betz-cells are seen shewing marked chromatolysis; there is also an increase of the satellite cells. This chromatolysis of the psycho-motor neurons, which give origin to the crossed pyramidal system of fibres, was more marked in the leg area than the arm area, and nearly all the cells were profoundly affected in this region, whereas in the face area none of the Betz-cells were so affected. It may therefore be assumed that the chromatolytic change was due to the destruction of all the fibrils forming the axon-process. The reason why the cells of the arm area were not universally affected, and those that did shew changes were not so markedly affected as the cells of the leg area, is no doubt because the axon-processes of many of the neurons had ended in terminal arborisations above the seat of the injury. Again, those that were affected with chromatolytic change had given off collateral fibrils before reaching the seat of the lesion, therefore there was not a complete destruction of the whole of the fibrils forming the axon. Polychrome methylene blue and eosin stain. Magnification, 500.

Fig. 2.—Section of the anterior cornu of the lumbar enlargement of the spinal cord of a monkey in which the lumbo-sacral posterior roots had been divided and the sciatic nerves subsequently cut and sutured on both sides. Later, semisection of the spinal cord on the same side as the division of the roots was performed. The object of the experiment was to see if the removal of stimulus by the posterior roots from the brain interfered with the regeneration of the nerves; it was found that it did not, but possibly this may be explained by the fact that even such lesions would not entirely deprive the anterior cornual spinal neurons of stimulus by cross paths in the grey matter. Complementary to the fact that regeneration was not interfered with, this section shews that the majority of the anterior cornual cells present a normal appearance; there are, however, two cells (*a*) which exhibit well-marked chromatolysis, swelling of the cell, and eccentricity of the nucleus, but a similar appearance of a few cells was seen on examination of the anterior horn on the side on which the only lesions were section and suture of the sciatic nerve. The inference is that the cause of the change of the two cells shewn in the plate is the section of the sciatic nerve, and that the other lesions mentioned did not in any way add to the changes in the spinal motor neurons. The conclusion may be arrived at that these spinal motor neurons have a trophic autonomy; a conclusion which is strengthened by the experiments of Ross Harrison. The section is 5  $\mu$  in thickness, was cut in paraffin and stained by polychrome methylene blue and eosin method. Magnification, 150.

*Fig. 1.*



*Fig. 2.*







recognise the lapse of time, for they thought that only about ten minutes elapsed between the warning "all up at once," and their arrival at the surface. In reality, nearly two hours had elapsed. Numbness of the fingers occurred to such an extent in one person that he unconsciously burnt his wrist and hand in the candle; this shews how profound was the effect upon sensory perception. Vomiting, headache, epileptiform seizures, and palpitation may result later. Violent clonic spasms, semi-comatose conditions followed by acute mania and later dementia have been described. A woman who killed her two children and committed suicide by inhalation of illuminating gas lived four days, and although the case was complicated by pneumonia and high fever, yet I am convinced that the changes I found in the ganglion-cells of the medulla were due to exhaustion owing to the anoxyaemia.

**The Appearance of the Nissl Granules in Pathological Conditions and their Significance.**—The appearance of the Nissl granules has long been one of the most valuable indications the neurologist possesses for the study of the changes of the ganglion-cells resulting from disease; and, provided that certain precautions are taken, valuable inferences can be drawn by comparing sections of normal nervous structures with those presumably diseased, after fixing, cutting sections, and staining the same by the Nissl method. There is a vast literature concerning the stainable bodies called Nissl granules. They were at one time believed to be an essential constituent of the living cell, but the researches of Hardy have shewn that there is a great difficulty in deciding to what extent structure demonstrable in the fresh or fixed state is the product of the chemical and physical changes which constitute the death changes, or is due to the action of fixatives. Moreover, Held and others have shewn that the *intra vitam* methylene blue method does not reveal Nissl granules in the cells. The stainable chromatic or chromophil substance, therefore, is probably not present in the living cell in the definite form in which we see it when the tissues are fixed and stained by the Nissl method. It must not, however, be assumed, therefore, that the method is unreliable as a means of studying the bio-chemical changes occurring in the protoplasm of the neurons, for, provided certain precautions are taken, it has proved most valuable in demonstrating functional and organic changes occurring in the nerve-cells as a result of (1) injury of the axon, (2) exhaustion from excessive fatigue, especially under the experimental conditions adduced on p. 210, (3) toxins circulating in the blood, and (4) hyperpyrexia.

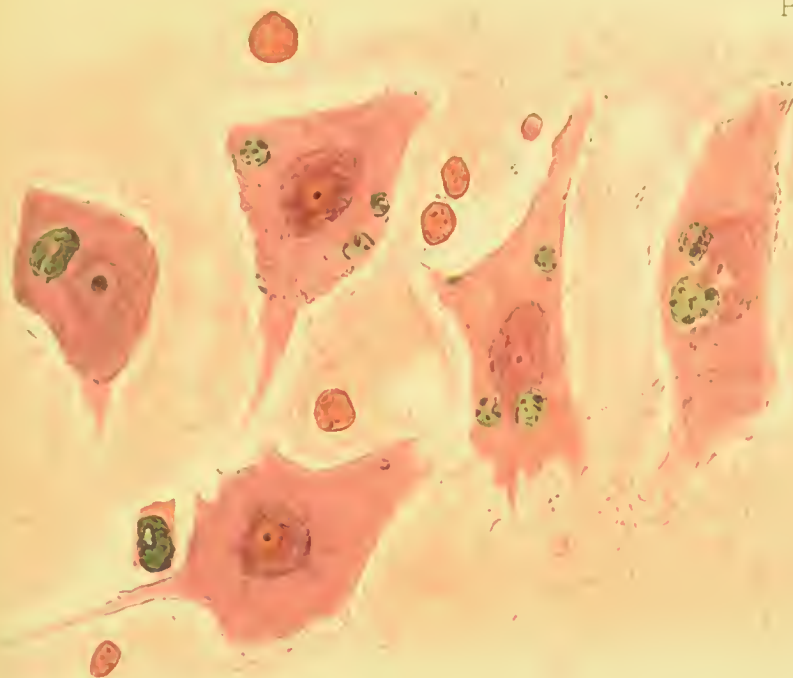
The large motor cells of the cord and brain are the best for studying the changes in the cell protoplasm, because in these structures the stainable substance appears in normal tissues after fixation as if it consisted of formed elements (Nissl granules) in the body of the cell and in the dendrons. I have always regarded these elements as being caused by a death change of the cell plasma whereby the nucleo-protein contained in it is thrown down as a fine precipitate, as myosin is precipitated from myosinogen. If this substance is abundant in the fluid plasma, it produces.

## PLATE IV.

FIG. 1.—Cells of the cornu ammonis from a case of rabies, shewing basophil-staining bodies within the cells. These bodies vary in size from 2 to 10  $\mu$  in diameter; they do not lie in the cell, for they can only be clearly seen in many instances by altering the focus. These bodies were regarded as the Negri bodies; it will be observed that the satellite cells around do not take the basophil stain. Mann's stain. Magnification, 750.

FIG. 2.—Giant pyramidal cell from the motor area of a case of amaurotic idiocy. The curious appearance of the base of the cell is characteristic of this disease; whether this is a change in the axon-cone or a flux of the cytoplasm is not apparent, but I have not seen this change in any other pathological condition of the brain. The red-stained dots throughout the deformed cell are due to a fatty substance; for if the sections are stained by Sudan III. or by Scharlach red they are stained deeply; moreover, the Weigert-Pal method stains the cells blue, owing to the minute globules of fatty matter taking the stain. Polychrome methylene blue and eosin stain. Magnification, 500.

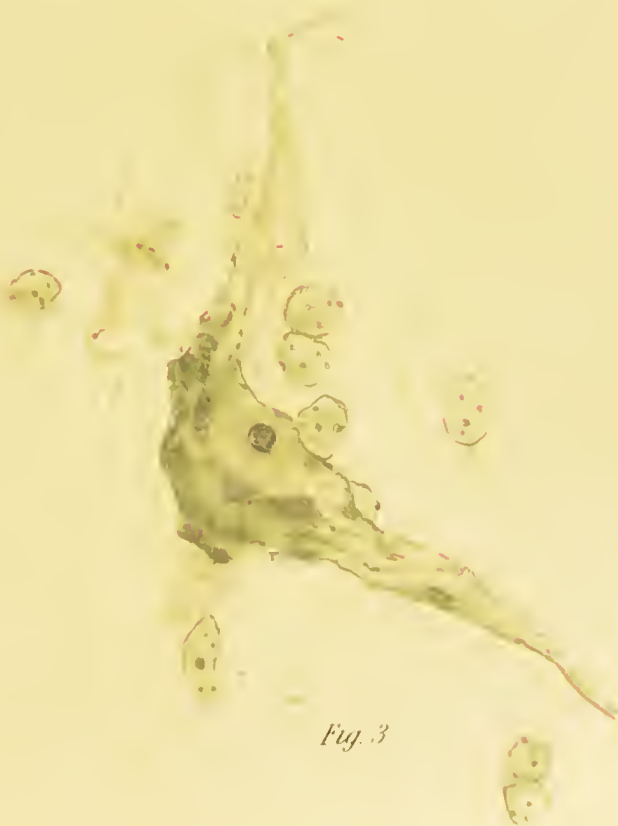
FIG. 3.—Giant pyramidal cell from the motor area of a monkey, in which a series of epileptiform convulsions had been induced by the injection of absinthe. The animal lived two hours. The cell shews chromatolysis and considerable shrinking; there are four satellite cells seen sticking to the exhausted ganglion-cell. The brain did not shew the same serous congestion, as in the case of epilepsy, Plate III., therefore the cells are not dropsical. Probably the change is one of exhaustion due to continuous discharge of energy in the production of the fits. Magnification, 850.



*Fig. 1.*



*Fig. 2.*



*Fig. 3.*





from microbial toxæmia there is a combination of central and diffuse chromatolysis.

Although in my experience it is possible in very many cases of toxic psychoses to demonstrate changes of structure in the cerebral cortex, the exact relation these bear to phenomena exhibited during life cannot even be conjectured. Each new method of studying the normal histology of the central nervous system, and the discoveries made thereby, have led not a few enthusiastic workers to predict a solution of the problems underlying mental action and even the still more difficult problem of diseases of the mind. Many investigators, working from different stand-points, have been and still are engaged in attacking this problem, but whilst there has been much histological detail and speculation regarding the correlation of histological changes with morbid mental states, but little rests upon the solid basis of scientific requirement. When such an accurate and experienced observer as Nissl, the inventor of the method which more than any other has been used with advantage for elucidating changes in structure of the nervous system, publicly states that we cannot be too sceptical in correlating cortical changes with mental diseases, and can only point to the probability that the plasma-cells of Marschalko constitute a specific lesion of general paralysis, we may well hesitate in accepting any cortical changes as evidence of specific toxic action. Even this is not pathognomonic, for plasma-cells are found in sleeping sickness, in syphilitic disease of the brain, and occasionally in encephalitis.

Not until we can eliminate a number of other factors is it safe even to assert that the changes are directly caused by a toxin introduced from without or engendered within the body. In the first place, post-mortem change must be discounted; my observations, however, are not affected by this factor, as the bodies were placed in a cold chamber very soon after death. Secondly, in the toxic psychoses death is so frequently complicated by pulmonary diseases, of which tuberculosis is the most common, especially in the subjects of dementia precox, epileptic imbecility, and melancholia. My experience indeed shews that the onset of mental symptoms in dementia precox and melancholia of adolescents so frequently coincides with the onset of tuberculosis that there must be a correlation indicating a depression of vital metabolism of the body generally and of the nervous system in particular, the latter being a result of an inherent defect of the nervous potential. It is impossible to say, therefore, whether the tuberculous toxin is a cause or an additional factor in the production of the mental phenomena. Certainly a vicious circle tends to be produced, for refusal of food and impaired nutrition, with slow and shallow respiration and feeble circulation, tend toward rapid progress of the infective process, and thereby an increased amount of tuberculous toxin is poured into the blood.

Though certain changes have been found in the cortex in dementia precox, they are probably not specific for this disease, nor the result of the tuberculous toxin, nor of the febrile state *per se*, but rather the

outcome of a deranged metabolism of the cortical cells in which microbial toxins, auto-toxins, or cyto-toxins may be the predisposing or exciting cause. If the insane do not die from acute or chronic pulmonary tuberculosis, secondary or terminal infections occur in a great majority of the remainder of the cases, giving rise to bronchopneumonia, pneumonia, gangrene of the lung, dysentery, bed-sores, and cystitis. Again, chemical restraint by the continued use of narcotising agents for convulsions and maniacal excitement may, as in the case of sulphonal, so alter the composition of the blood as to depress the metabolism of the cortical cells and so be responsible for the histological changes. Moreover, in cases with prolonged convulsions, as in the status epilepticus and in some cases of general paralysis, the mechanical conditions are such as to produce a vicious circle terminating in progressively increased vascosity of the blood in the cortex, especially of that portion supplied by the carotid arteries, the veins of which drain into the longitudinal sinus. In fact, a pure case free from complications and intercurrent affections, such as respiratory failure of considerable duration, asphyxia, cardiac failure, or some secondary infection, is rarely to be obtained. Thus, cases of sudden death arising from injury, suicide, accident, or some other cause, would be specially valuable for determining the relation of acute and chronic intoxications to lesions of the cerebral cortex. However, if a patient who has died of one of these various conditions has not presented during life any delirium or mental confusion, and the cortical structures present no abnormality, whereas in another patient delirium, mental confusion, or even insanity occurred, and chromophil changes of the cortical cells are found, we are justified in correlating the absence of mental symptoms in the former case with the absence of these changes, and the existence of mental symptoms in the latter with such changes. But we are not, therefore, justified in asserting that poisons introduced from without, microbial toxins, or auto-toxins can produce specific lesions *per se*. The metabolic reactions of systems, groups, and communities of neurons to their environment may be altered by the toxic condition of the blood. An actual chemical combination may occur as in the case of tetanus toxin, which has an elective affinity for the grey matter in the spinal reflex arc. Similarly, other poisons may have an elective affinity for certain groups or systems of neurons with specific functions, thus accounting for specific functional disturbances resulting from particular poisons. It is generally believed and widely taught that auto-toxins are the cause of many psychoses; but we are entirely ignorant of their source, the manner in which these poisons act, and of their chemical properties. It is probable that poisons act upon the neuron by interfering with its normal metabolism either by increasing dissimilation processes with an increased expenditure of its oxygen-store and a liberation of neural energy, thus acting as excitants, or by interfering with its assimilating processes, and thus causing paralysis of function.

The fundamental basis of the study of toxic psychoses in relation to cortical lesions is a knowledge of the chemistry of the normal neurons





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and the metabolism of the nervous system. By a further study of histo-chemical methods and selective stains it may be possible to differentiate the essential chemical substances of the neuron, to ascertain the changes which these substances undergo during functional activity, and eventually to separate and prepare the substances for the determination of their exact chemical composition.

The only cortical lesion of toxic origin which presents a group of morphological changes quite specific in their characters is general paralysis. This disease is almost universally regarded as being syphilitic in origin. It is desirable to draw a comparison between the structural changes found in the brain of a paralytic and of a chronic alcoholic dement.

*General Paralysis.*—The extraordinary recovery from seizures of general paralysis suggests that a portion of the symptoms may be due to functional disturbance of the cortex brought about by circulatory derangements. A large number of the cortical cells in general paralysis shew acute changes due, no doubt, to vascular disturbances. Many exhibit the swollen, dropsical condition of the functional change which occurs in the brain rendered anaemic by ligation of arteries (*vide* p. 215); these cells, we have seen, are capable of recovery; others present acute necrobiotic change, and are incapable of recovery. The cells psycho-motor in function are hyper-excitabile, and give rise to epileptiform convulsions in the stage of irritation preceding death. These acute changes in the cells are specially met with in rapid cases in which there have been many seizures. If the spinal cord be examined by the Marchi method the crossed pyramidal tracts will generally be found to contain degenerated fibres, in a measure proportional to the number and severity of the fits. The axons of these fibres are prolongations of those psycho-motor cells which shew a necrobiotic change. When the fits have been unilateral, the degenerated fibres will be found in much greater numbers on the same side as the convulsions. After death it will usually be found that the hemisphere opposite to the side on which the fits occurred weighs much less when stripped of its membranes than the hemisphere of the same side. I have seen as much as 100 grams difference. This is doubtless due to a venous stasis, which I have occasionally seen progress to such an extent as to cause thrombosis first of one great anastomotic vein, then of the other.

Again, when there is marked alteration of speech in general paralysis, the left hemisphere is very liable to be more affected than the right, although in my experience Alzheimer is quite correct in asserting that the cortical lesions of general paralysis differ from those of arteriosclerosis and syphilitic disease of the brain in being universal; yet there is not the slightest doubt that the naked-eye appearance shews that those regions of the cortex in which arterial anaemia and venous stasis are most likely to occur exhibit the most thickening, congestion, and opacity of the pia-arachnoid, the most adhesions, and the greatest wasting of the convolutions. The most characteristic naked-eye change in general paralysis is

the granular endyma of the ventricles, especially the fourth. In no other disease except brain syphilis is this change met with.

The characteristic microscopical features of general paresis are : (i.) Infiltration of the pia-arachnoid membranes with lymphocytes and plasma-

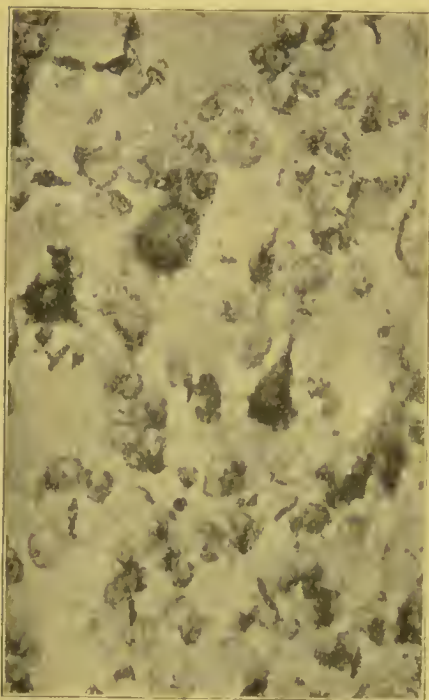


FIG. 48.—The acute cell changes in general paralysis; the swollen droopical condition of many of the small pyramidal cells closely simulates the appearance presented by these cells in experimental ligature of the arteries in animals; presumably these changes are in part due to vascular stasis and anaemia. Magnification, 250 diameters.

cells which tend to undergo regressive changes. (ii.) Presence of rod cells (*Stäbchenzellen* (Alzheimer)). (iii.) Appearance of increased vascularity, owing to the endothelial cell proliferation of the capillaries and small vessels; sprouting and the tendency to the formation of new capillaries; degenerative changes in the walls of the small arteries and veins, and infiltration of the *lymphatic sheaths of the vessels with lymphocytes and plasma-cells*. This condition, practically speaking, is not met with in any other diseases except cerebral syphilis and sleeping sickness; in the latter the lymphocytic accumulation is even more pronounced and much more widespread through the whole central nervous system. In the chronic cases of sleeping sickness the granule cells and large macrophages containing altered pigment are much more numerous than in paresis. (iv.) The glial tissue shews more active proliferation than in any other disease, the large spider-cells being especially numerous and well defined, particu-

larly in the superficial layers of the cortex (Fig. 46). (v.) The ganglion-cells have lost their columnar arrangement, they are distorted in shape, displaced in position, and may be observed in all stages of acute, subacute, or chronic destructive decay. The extent of this destruction of neurons may be correlated with the depth of the dementia (*vide* Figs. 47, 48, 49). (vi.) The fibres are proportionally atrophied, and the first to be affected are the association systems, especially the tangential and supraradial. The Marchi method may shew numbers of recently degenerated fibres. (vii.) The frontal region shews as a rule the most advanced changes, and should therefore be examined in doubtful or atypical cases. Typical vascular, cellular, and glial changes may be found there when not present elsewhere. In many tabo-paralytic cases, especially those with optic atrophy, I have sometimes found the occipital cortex relatively more affected than other parts of the brain.

*Alcoholic Psychosis.*—There is no specific lesion of the brain in acute



or chronic alcoholism. Many persons who are chronic drunkards die without any recognisable cerebral change; the degree in which the brain is affected in the one case and the peripheral nerves in another in all probability depends upon inherent neuropathic or psychopathic tendencies of the individual. Since experiments upon animals are not followed by changes in the brain similar to those met with in chronic alcoholic psychosis, it is probable that alcohol does not act directly upon the neural elements. There is usually an associated microbic toxæmia or auto-toxæmia which deranges metabolism and interferes with the normal functions of the organs of the body; in consequence, the unstable neural elements are unable to adapt their metabolism to the altered and toxic ambient medium. Dr. Ascherson found that in 20 (16.6 per cent) of his cases the mental symptoms of Korsakow's disease followed immediately an attack of delirium tremens, an observation which supports the view of Bonhöffer, Kräpelin, and others, that Korsakow's disease and delirium tremens are but different forms of the same affection. Both are essentially late manifestations of alcoholism, and occur either as a result of microbic infection or pathological changes in such organs as the liver and intestinal tract.

I have found in a case of delirium tremens, which after a week terminated in pneumonia, coma and death, general congestion and hyperæmia of the brain substance; microscopical investigation showed specially marked changes in the cortical cells which the febrile state would not account for. The cord and medulla oblongata, the white matter of the cerebellum, the basal ganglia, internal capsule and corona radiata, and especially the optic radiations when stained by the Marchi method, exhibited numbers of black granules of varying size and many

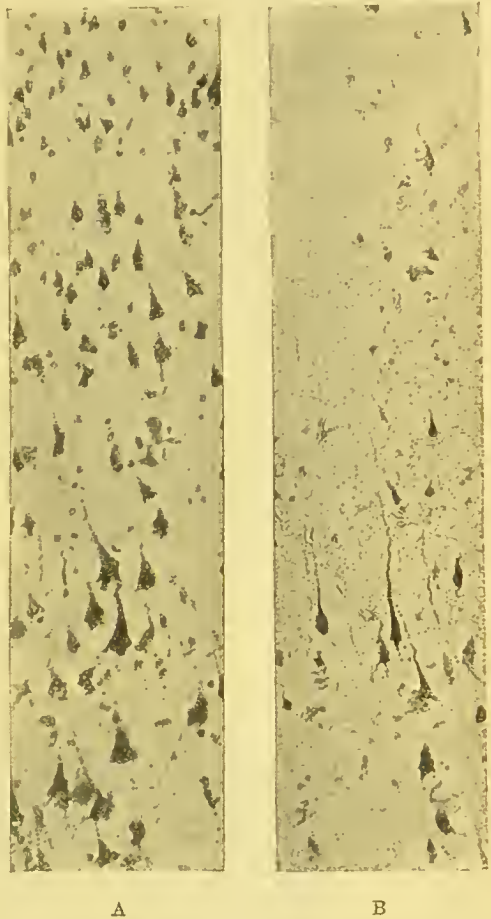


FIG. 40.—A. Section of the prefrontal cortex of the brain of a man who died from a stab in the heart; this normal cortex, as regards number and shape of cells of the pyramidal layer, is for comparison with B. B. Section of the brain of a general paralytic girl, aged fourteen at death, the subject of congenital syphilis; relatively only a few pyramidal cells are seen. Observe the corkscrew appearance of the apical processes. Magnification, 150.

degenerated myelinated fibres. Some capillary haemorrhages were found scattered about in various regions of the grey matter of the basal ganglia and medulla and in the optic thalamus; a few sections of vessels shewed the lumen filled with a fibrinous clot, consisting of filaments of fibrin and white corpuscles. It was probable that thrombosis of the small vessels accounted for the Marchi degeneration. A similar condition, only very much more pronounced, both as regards haemorrhages and degenerations, I have found in two cases of subacute carbonyl of nickel poisoning, and one case of coal-gas poisoning. All these cases were complicated by pneumonia. It is therefore probable that the toxin of the pneumococci played a considerable part in the neural changes by causing vascular thrombosis and haemorrhages.

A case of Korsakow's psychosis in a female chronic drunkard with symptoms of polyneuritis of all four limbs, of one month's duration, was admitted to Charing Cross Hospital with loss of the naso-labial fold on one side, sluggish reaction of the pupils, loss of knowledge of time and place, loss of memory for recent events, and personal illusions; tachycardia supervened, the patient became at first delirious, then comatose, and died on the fourth day. At the necropsy intense congestion of the brain was observed and subpial cortical haemorrhages; scattered through the cortex were numerous patches of what appeared like red softening. Microscopical examination shewed that these foci were caused by the aggregation of recent capillary haemorrhages varying in size from a small to a large pin's head (Fig. 50, A). The nuclei of the endothelial cells of the small vessels were swollen and proliferated, and doubtless this condition and the cardiac failure had caused the haemorrhages. Besides this, the cortex shewed fibre-, cell-, and glia-changes of moderate degree. It is also interesting to note that the vagus nerves were degenerated, and that there was marked fatty degeneration of the heart. The changes found in 6 other cases which I have examined were similar qualitatively but not quantitatively; there was a certain parallelism between the degree of dementia and the amount of cortical change. The peripheral nerves were in all cases affected, but not to the same degree. In some the cortical changes predominated; in others the neuritis.

Some cases of Korsakow's psychosis are difficult to differentiate clinically from general paralysis:—

A female, aged fifty-three, was admitted to the asylum with symptoms of one month's duration, and a history of chronic drunkenness. There were the usual symptoms of alcoholic dementia, but in addition she had had several fits. There were grandiose delusions of wealth, sluggish pupils, and exaggerated knee-jerks. She died two months after admission from bronchitis and emphysema. At the necropsy there were no signs of cerebral wasting, and nothing abnormal to the naked eye save a slight opacity and thickening of the membranes in the fronto-parietal region. The brain was normal in weight, no excess of fluid, and but little loss of weight on stripping the hemispheres. Only a very few fine granulations in the lateral sacs of the 4th ventricle were found. The microscopical changes present in the cortex corresponded with those found in the other



A



B

FIG. 50.—A. Section of the brain from an acute case of polyneuritic psychosis shewing haemorrhages in the superficial layers of the cortex. B. Section of the brain from a case of chronic polyneuritic psychosis shewing a large pyramidal Betz-cell with chromatolysis extending upwards from the axon-cone of origin; the nucleus is eccentric.

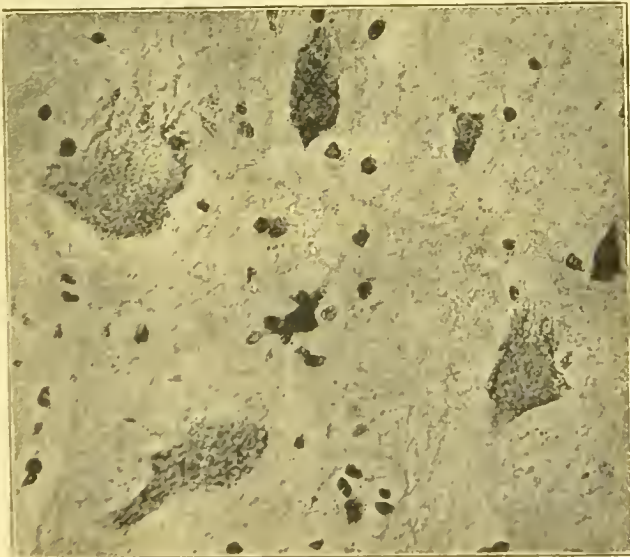


FIG. 51.—Section of the top of the ascending frontal convolution from a brain of a case of the katatonic form of dementia praecox, shewing chromatolytic changes and eccentric nucleus of the large Betz-cells. Magnification, 500.



cases, but were more pronounced. (i.) The membranes were thickened and congested, but there was no infiltration with lymphocytes and plasma-cells, and no regressive changes. (ii.) There was a considerable atrophy of the tangential and supraradial fibres and, to a less degree, of the inter-radial and radial fibres (*vide* Fig. 53). (iii.) The cells were arranged in columns and there was but little distortion of the normal lamination and cell arrangement. There were considerable degenerative changes of the cells of the pyramidal layer; in many the

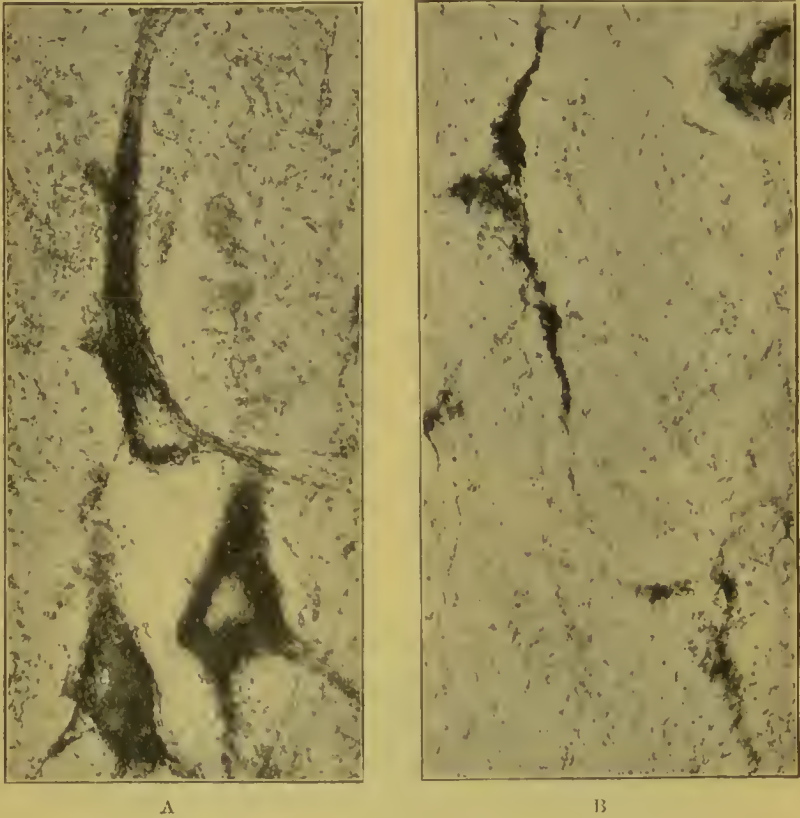


FIG. 52.—A. Large pyramidal cells from the same region of the brain of the same case as those of Fig. 51, stained by the Cajal fibril method. Magnification, 500. B. Similar cells from a case of advanced general paralysis shewing complete destruction of the neuro-fibrils. It must not be inferred that all the cells even in an advanced case of general paralysis would shew such a profound change; all grades of decay would probably be seen from slight or even unrecognisable change to the complete decay such as this specimen indicates. No such change as this would be seen in dementia precox or alcoholic psychosis. Magnification, 500.

apical processes were not visible; the edges of many cells were crumbled, not a few were completely disintegrated, and quite half of them stained poorly and diffusely. The large Betz-cells presented an appearance like that seen in the anterior cornual cells in polyneuritis. There was a central chromatolysis, the nucleus often swollen up, clear, and eccentric (*vide* Fig. 50, B). All the layers of the cortex were affected. (iv.) There was a considerable glial cell proliferation, and a felt-work of spider-cells in the molecular layer. In the remainder of the grey matter of the cortex there was a proliferation of the glial tissue, but the fibres were not so large, numerous, or distinct as in general paralysis. In the



subjacent white matter there was a considerable proliferation of glial nuclei.  
(v.) Vessels.—The vessels presented an entirely different appearance to those

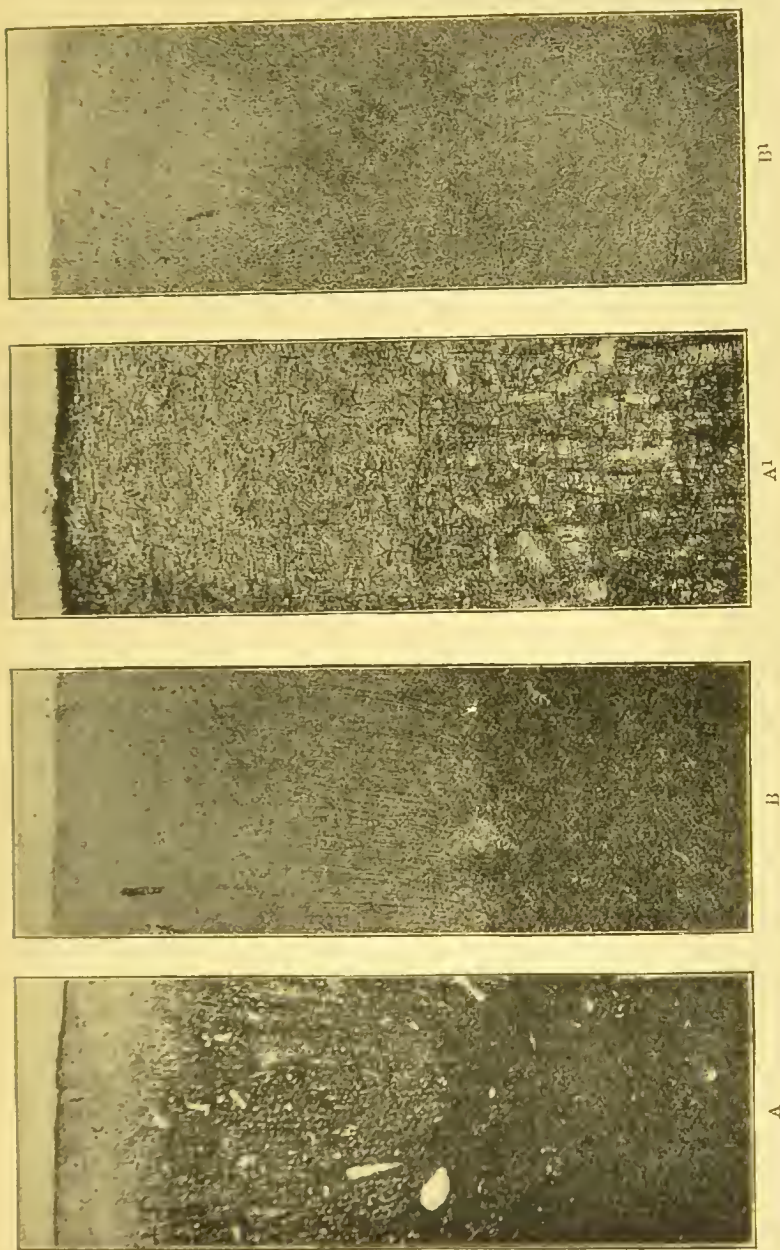


FIG. 53.—These figures are photomicrographs of the cerebral cortex with a low power and a high power of a section of a normal cortex A, and of the cortex from a case of advanced alcoholic dementia B, B1. The specimens were stained by the Weigert-Pal method to display the fibres in the two sections of cortex. It will be observed that there is a much greater wealth of fibres in A than in B, and that the loss of fibres in B is especially marked in the superficial layers. If A1 be compared with B1 it will be observed that in this case of alcoholic dementia there is almost a complete disappearance of the fibres in the tangential, supradial, and inter-radial association systems. It must not, however, be thought that this condition is a usual occurrence; as a matter of fact it is extremely rare to find such a marked change in alcoholic dementia.

of general paralysis. Nowhere could I find in any of the six cases a similar accumulation of lymphocytes and plasma-cells in the lymphatic sheaths. There

were swelling and proliferation of the endothelial nuclei, there was no evidence of sprouting or tendency to form new capillaries, and there were no rod-cells.

**Hyperpyrexia.**—The study of the lesions of the nervous centres due to hyperpyrexia is of great interest from a theoretical as well as from a practical point of view; from the former because an exact knowledge of the nature of the lesion might be able to throw some light upon the pathological process and the relation of the same to the clinical symptoms which accompany hyperpyrexia; from the latter because it would indicate the direction of treatment. Goldscheider and Flatau, who for the first time described lesions of the nerve-cells in the rabbit caused by experimental hyperthermia, came to the following conclusions: (1) If the temperature remained about  $106.7^{\circ}$  F., the cells of the spinal cord examined by Nissl's method presented no appreciable modifications. (2) If the temperature exceeded  $109.5^{\circ}$  F., the lesions of the nerve-cells of the spinal cord were very definite, extending throughout the whole of the grey matter. (3) The duration of the experimental hyperthermia was a very important factor in the production of the lesions, for if the animal be kept for some hours between  $107^{\circ}$  and  $108^{\circ}$  F., the same effect on the nerve-cells is produced as occurs in a much more rapid manner when the temperature is raised to  $109.5^{\circ}$  F., namely, swelling of the cell and its processes; diffuse staining of the whole neuron with disintegration of the chromophil elements still persisting to some extent as if the outer portions of the cell were more affected than the central. The nucleus has an irregular and often an angular appearance.

Marinesco found that if artificial hyperthermia in animals be produced, so that the temperature is raised to  $116.6^{\circ}$  F. in the rectum, the animal dies in thirty minutes with characteristic changes in the nerve-cells. He also remarked that these changes occur at a lower temperature when the duration is increased. In 5 cases of hyperpyrexia occurring in the human subject which I have examined, and in which the temperature reached  $109^{\circ}$  F. or more, I have found the same biochemical change revealed by the Nissl method in all the cells of the central nervous system. I have, however, met with cases of status epilepticus in which the temperature was from  $107^{\circ}$  F. to  $107.5^{\circ}$  F. for a short time without shewing this change. Again, I have seen in one case a moderate degree of chromatolysis and diffuse staining in prolonged pyrexia varying from  $103^{\circ}$  to  $106.5^{\circ}$  F.; as this was in enteric fever, it is quite possible that the change was due to the influence of the toxin. In fact, in most of the human cases the changes could be ascribed to the conditions which produced the fever and not to the influence of the increased temperature of the blood. Some of the cases which I have examined, however, were sudden; thus, one was probably sunstroke, in another there was haemorrhage into the spinal canal and the base of the brain in general paralysis, and another was a case of sleeping sickness. (*Vide* Vol. I. Plate VI. Figs. 2, 3.) I have examined the nerve-cells in many cases of septic poisoning and other diseases, but

I have never seen this change unless there was either hyperpyrexia or prolonged high fever. The fact that experimental hyperthermia in animals produced this bio-chemical change in the protoplasm of the cell indicates that it is the altered temperature of the blood which is the cause in the human subject of these changes. Another point is that if the sections are stained with methylene blue and safranin, the protoplasm is stained a uniform dull purple instead of being differentiated. Now we have seen that the healthy cell shews a differentiation of staining; the Nissl granules which have been proved to be a nucleo-albumin are no longer visible in hyperpyrexia; and there is no longer the differentiation of a stainable and an unstainable substance with basic dyes. The fever, therefore, must have been accompanied by the profound modification of the protoplasm of the cell. There are two points to be considered in this: (1) that a temperature of  $109.5^{\circ}$  F. can induce this coagulative process and death of the protoplasm rapidly, and also that it affects first and most markedly the periphery of the cell; and (2) that prolonged high temperature of from  $107^{\circ}$  to  $108^{\circ}$  F. will produce the same coagulative process. Professor Halliburton has shewn that there are three proteins in nervous matter: (a) a nucleo-globulin which is coagulated at  $116.6^{\circ}$  F. ( $47^{\circ}$  C.); (b) a nucleo-protein which is coagulated at  $132.8^{\circ}$  F. ( $56^{\circ}$  C.); and (c) a neuroglobulin which is precipitated at  $167^{\circ}$  F. ( $75^{\circ}$  C.); and that these three bodies can be separated out by fractional coagulation. We see, then, how it is that Marinesco found that animals in which the temperature is raised to  $116.6^{\circ}$  F. ( $47^{\circ}$  C.) died almost immediately with changes in the cells indicating coagulation in the protoplasm. No doubt this neuroglobulin is precipitated at once, and it occurred to me that if a solution of neuroglobulin were subjected to long heating, it would coagulate at a much lower temperature. I mentioned the matter to Professor Halliburton, who was of the same opinion, and we therefore made experiments on this subject, and found that prolonged heating for four hours, for example, will cause coagulation of the neuroglobulin at a temperature of between  $107.6^{\circ}$  and  $109.4^{\circ}$  F. ( $42^{\circ}$  to  $43^{\circ}$  C.). Moreover, Professor T. G. Brodie and Dr. Richardson have shewn that in frog's muscle the tissue loses its irritability at that temperature at which coagulation is induced first in one of its constituent proteins. We have thus a chemical explanation of the cause of the death of the protoplasm, also of the changes manifested by it as regards staining. Experimentally Goldscheider and Marinesco have found that a certain degree of this coagulative change may take place without death of the cells; for when they produced artificial hyperthermia in animals for only a short time and then killed them, this coagulative process was seen to have begun. But since these animals would have lived had they not been killed for the purpose of examination, we may suppose that a certain degree of bio-chemical change, associated with the coagulation of neuroglobulin, may take place without destroying the protoplasm to such a degree as to render it incapable of recovery. I think this entirely coincides with, and



explains, the remission of symptoms, the return of consciousness, and the recovery which often takes place in some forms of hyperpyrexia when the cold-bath method is resorted to without delay.

It is a matter of speculation whether structures later developed and functionally more highly differentiated, as the cells of the cerebral cortex, are specially susceptible to fever and succumb more readily under it. Possibly high temperature of the surrounding blood and lymph is more readily felt by the small cells of the superficial layers of the cortex on account of the increased surface exposed, and delirium followed by coma may be the result of this, although the vital centres in the medulla may still be able to perform their functions.

The diffuse staining of the cells indicates a diffusion of the nucleo-protein through the substance of the cell body and its processes. We may suppose, therefore, that the essential achromatic fibrillar substance is killed and that the nucleo-protein which is normally contained in the reticulum of the cell in solution has soaked into the achromatic substance and given the protoplasm the uniform staining which, when once general, is quite characteristic of hyperpyrexial death, as I have been able to verify in several instances. These facts, pointing to an actual biochemical change involving the death of the protoplasm when the temperature remains for some hours above 109° F., support Professor Osler's view that cases of paradoxical temperature occurring in women and termed "hysterical hyperpyrexia" are frauds as a rule, although he states that other cases have to be accepted, the explanation of which is impossible under known rules—in fact, it is quite conclusive that a temperature above 114° F. is incompatible with life, even for a short time. It has already been pointed out on p. 212 that hyperthermia interferes with constructive metabolism while increasing destructive metabolism, and this may be an explanation of the disappearance of the Nissl granules rather than a coagulative process. I have found in the status epilepticus a diffuse staining of the cells similar to that seen in hyperpyrexia (Plate III.): this protoplasmic change may be accounted for by the energetic processes of dissimilation associated with cortical discharge accompanied by an alteration of the ambient medium, viz. excess of CO<sub>2</sub> with proportional diminution of oxygen and hyperthermia. There is thus a conspiracy of pathological factors all interfering with the life of the cell and its power of assimilation and repair of waste. A change in the osmotic relations of the cell to the ambient medium occurs and it swells from imbibition of water.

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THE LINKING TOGETHER OF THE NEURONS. — *The Spinal Cord and its Connection with the Brain.*—The neurons are linked together into

functionally correlated systems and communities. They belong to three groups,—afferent, efferent, and association,—the last-named being by far the most numerous. As the nervous system becomes more complex in function, so the association neurons become more numerous and complex as compared with the neurons of the projection systems. The cerebral cortex of the human brain consists in great part of association neurons, but even in the grey matter of the spinal cord the association neurons are more numerous than the spinal motor neurons. These association neurons, termed proprio-spinal neurons by Professor Sherrington, serve to link up the segments of the grey matter at different levels, and thus integrate the action of the segments. Besides these neurons there are others in the grey matter, and they are very numerous, small, and with many fine processes; the axons of these neurons do not leave the grey matter. These are termed intercalary neurons, and probably von Monakow is correct in asserting that these intercalary neurons, second type of Golgi, always intervene between other neurons—afferent, efferent, and association. They are always very numerous wherever sensory terminal arborisations exist.

**The Spinal Cord as an Organ of Transmission.**—The spinal cord may be considered, in the first place, as a collection of segmental autonomic afferent and efferent neurons, each segment being connected with a posterior spinal ganglion from which it receives fine and coarse fibres; the former are in connexion with superficial cutaneous structures and the latter with deep structures,—joints and tendons, bones and muscles. The fine fibres end in the grey matter of the posterior horn of the same segment—Lissauer's tract—and form the afferent path of the reflex arc in the superficial skin reflexes. The coarse fibres arising from afferent neurons innervating the deep structures are of three kinds: (1) Short spinal; after a short passage through the posterior columns they enter by the root-zone the grey matter at the base of the posterior horns forming the afferent path for the segmental deep reflexes. (2) Medium-length cerebellar; these fibres, after running upwards through several segments or more in the postero-external column, arborise around the cells of Clarke's column; they connect with the system of afferent spinal cerebellar neurons. (3) Spino-bulbar; these are long fibres, and form the columns of Goll and Burdach (*vide* Plate V.).

The two latter systems of neurons convert the spinal cord into an organ of transmission of afferent impulses from the periphery to the brain. The spinal cord is also an organ of transmission of efferent impulses from the brain to the periphery. The cells of origin of these neurons are situated above the spinal cord; they form three different systems:—

(1) Bulbo-spinal; the vestibular nerve terminates in a mass of grey matter in the floor of the bulb known under the various names of Deiters' nucleus, vestibular nucleus, nucleus of Bechterew. From the neurons of this nucleus fibres pass down the antero-lateral column to end in arborisations around all the spinal motor neurons. (Fibres also pass

into the posterior longitudinal bundle to end in the ocular nuclei.) These fibres are also termed vestibulo-spinal, because they convey impressions from the semicircular canals to the cervical, dorsal, lumbar, and sacral spinal motor neurons of the same side (*vide* Fig. 54). These vestibular impressions play a very important part in the maintenance of the spinal tonus of muscles.

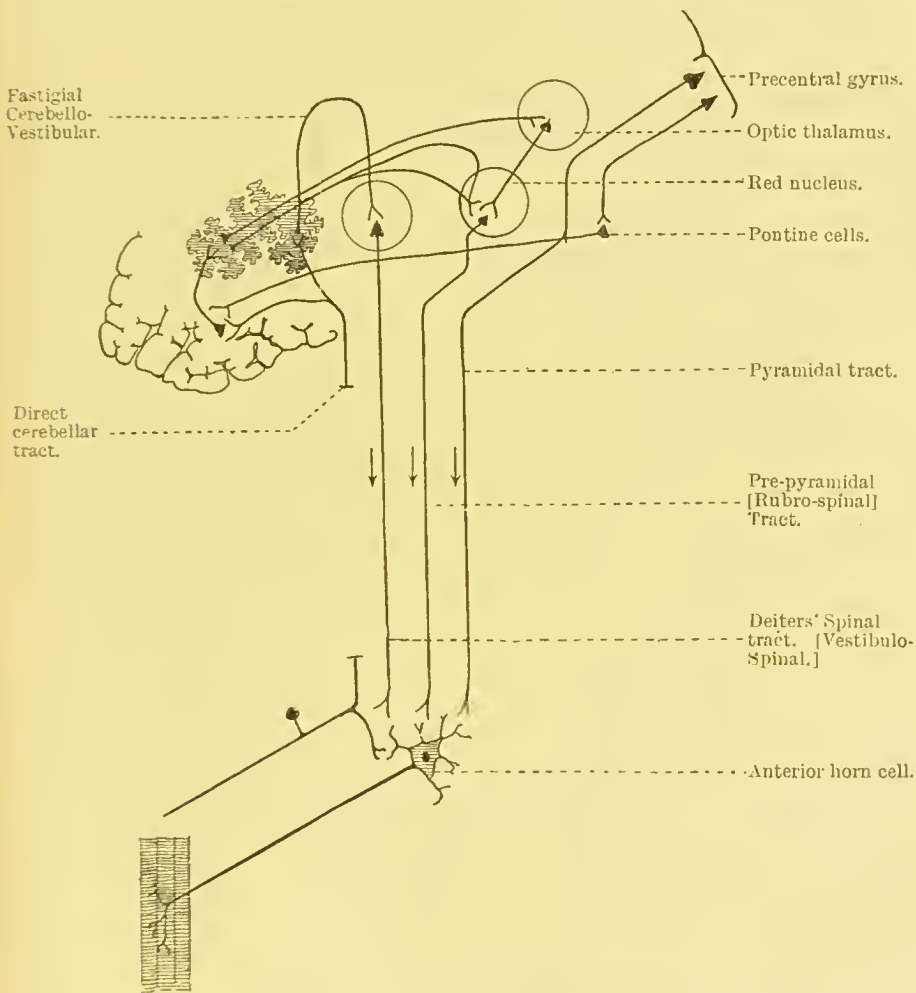


FIG. 54.—Diagram to illustrate the efferent systems of the cerebrum and cerebellum.

(2) Mesencephalo-spinal.—The most numerous and important set of mesencephalic fibres arise from the red nucleus; they decussate as shown in Fig. 54, and pass all the way down the lateral column of the cord, arborising at the base of the anterior horn. This system of fibres is therefore termed rubro-spinal; there is, besides, another system of fibres which belong to the posterior longitudinal bundle, and have their cells of origin in a mass of grey matter near the posterior commissure. The

upper connexions of these two masses of grey matter are not very well known, but according to van Gehuchten it is probable that they are in direct or indirect connexion with the optic fibres. These mesencephalo-spinal bundles of fibres transmit to the spinal motor neurons excitations from the optic tracts and help to maintain tonus (*vide* Fig. 54).

(3) Tecto-spinal.—A system of fibres arises in the corpora quadrigemina; some of these fibres can be traced down to the sacral region, and it is presumed that they may exercise control over the bladder and rectum.

(4) Cortico-spinal.—The grey matter of the ascending frontal convolution contains the large Betz-cells, and these cells give origin to the crossed and direct pyramidal tract fibres. These fibres are therefore called cortico-spinal (*vide* Plate V.).

The spinal cord, as an organ of transmission of impulses to and from the brain, is therefore exclusively formed by long fibres of its white substance; they consist, as we have seen, of two groups ascending and descending. The ascending or afferent system is composed of: (i.) Afferent fibres of the posterior columns forming the first segments of the cerebellar afferent systems. (ii.) Ascending fibres occupying the periphery of the lateral columns and forming two groups: (a) Antero-lateral, or Gowers' tract, consisting largely of crossed fibres which have three terminal stations, namely, the majority, which go to the valve of Vieussens and the vermis of the cerebellum, hence this tract is often called the ventral cerebellar; a few end in the lateral nucleus; some end in the corpora quadrigemina; a very few end in the pulvinar of the optic thalamus. (b) Direct cerebellar, or dorsal cerebellar; these pass into the restiform body and the inferior peduncle to end in the vermis.

The descending, or efferent system, is composed of: (i.) cortico-spinal: descending fibres of the crossed and uncrossed pyramidal tracts of the anterior and lateral columns; (ii.) vestibulo-spinal; (iii.) rubro-spinal; (iv.) tecto-spinal; (v.) (?) posterior longitudinal bundle fibres.

If at any level we imagine all these fibres of transmission removed, there remains the spinal cord of the segmented animal. Each of the thirty-one segments contain reflex arcs of afferent and efferent neurons integrated by proprio-spinal neurons, the fibres of which surround the grey matter. In this we could observe: (1) The grey matter of the spinal cord, but it is a grey matter considerably simplified in its structure not only by the disappearance of the cells of origin of all the spino-cerebellar fibres, but still more by the disappearance of all the terminal fibrils of the descending efferent systems. (2) A zone of white substance surrounding all parts of the grey matter and formed by fibres belonging to the spinal cord proper; these are ascending and descending systems of fibres which serve to associate or integrate the segments. These systems of fibres serving to integrate the reflex arcs are termed by Prof. Sherrington "proprio-spinal." (3) The peripheral nerves, comprising the centripetal fibres of the posterior roots and the centrifugal fibres of the anterior roots.



The grey matter of the anterior and posterior horns is the place where the cells of origin of the motor nerves and of the spino-spinal association-fibres are situated. In a complete transverse lesion of the spinal cord the fibres of transmission to and from the brain are completely put out of action below the lesion; the patient responds to cutaneous excitation unconsciously; moreover, he has no power to prevent, modify, or check the reaction to the stimulus. These reactional movements of exclusively spinal origin are termed reflex movements. Sometimes so exaggerated is the spinal reflex activity in a case of flaccid paraplegia that reactions occur without any apparent cutaneous excitation. But there always is a cutaneous excitation, although it may be very slight, such as that which would be caused by displacement of air or movement of the bed-clothes.

Plate V., modified from von Monakow, explains the linkage of the neurons and the path taken in a conscious sensation of the skin surface followed by a motor reaction; it also shews diagrammatically the associa-

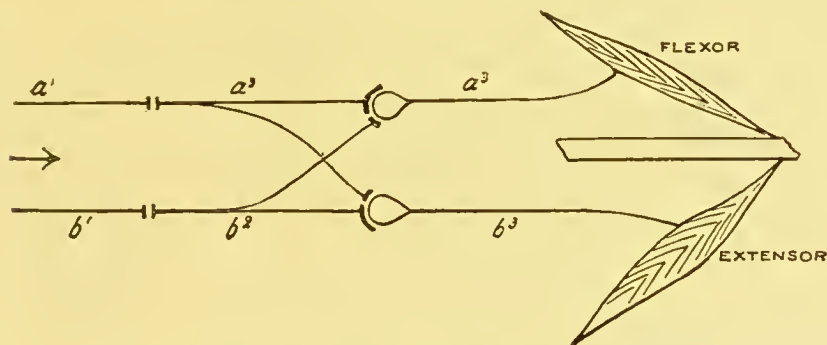


FIG. 55.—Diagram illustrating the "drainage theory." (M'Dougall.)

tion with other regions of the cortex by which memory-images of past experiences could be called up relating to the objects causing the sensation, the name of the object, etc. In this diagram the intercalary neurons, second type of Golgi, are represented red; their axons never leave the grey matter; these neurons always form a connecting link between the neurons of the first type of Golgi, and they serve an important function in the synapse. It will not be out of place here to consider an important hypothesis put forward as to the synapse and the part played by these intercalary neurons. This hypothesis is known as the "drainage theory," and was formulated by Dr. M'Dougall to explain attention. In attention there is concentration of nervous discharge along particular and limited chains of neurons or functionally correlated systems, and withdrawal from the remainder. This presupposes a labile substance productive of nervous energy which passes along certain lines of discharge, and Dr. M'Dougall postulates a substance "neurogen" which exists at the synapse and liberates energy. Now, if we represent diagrammatically (Fig. 55) two antagonistic neuro-muscular mechanisms, for example,

## PLATE V.

Modified scheme, after von Monakow, to shew the connexion of the afferent and efferent tracts of sensory and motor neurons, and the association neurons (black) by means of the intercalary (2nd type of Golgi) neurons (red).

A = Association neurons.

B = Nuclei of Goll and Burdach connecting neurons with the cerebellum, mesencephalon, and TH optic thalamus; here there is a relay of sensory neurons to every part of the cerebral cortex.

C = Pons. The pyramidal cells of the frontal portion of the brain send fibres (cortico-pontine) to arborise around cells in the pons; there is a relay in the pons, and the impulses pass down to the anterior horn cells as shewn in the diagram.

S = Sensory protoneuron.

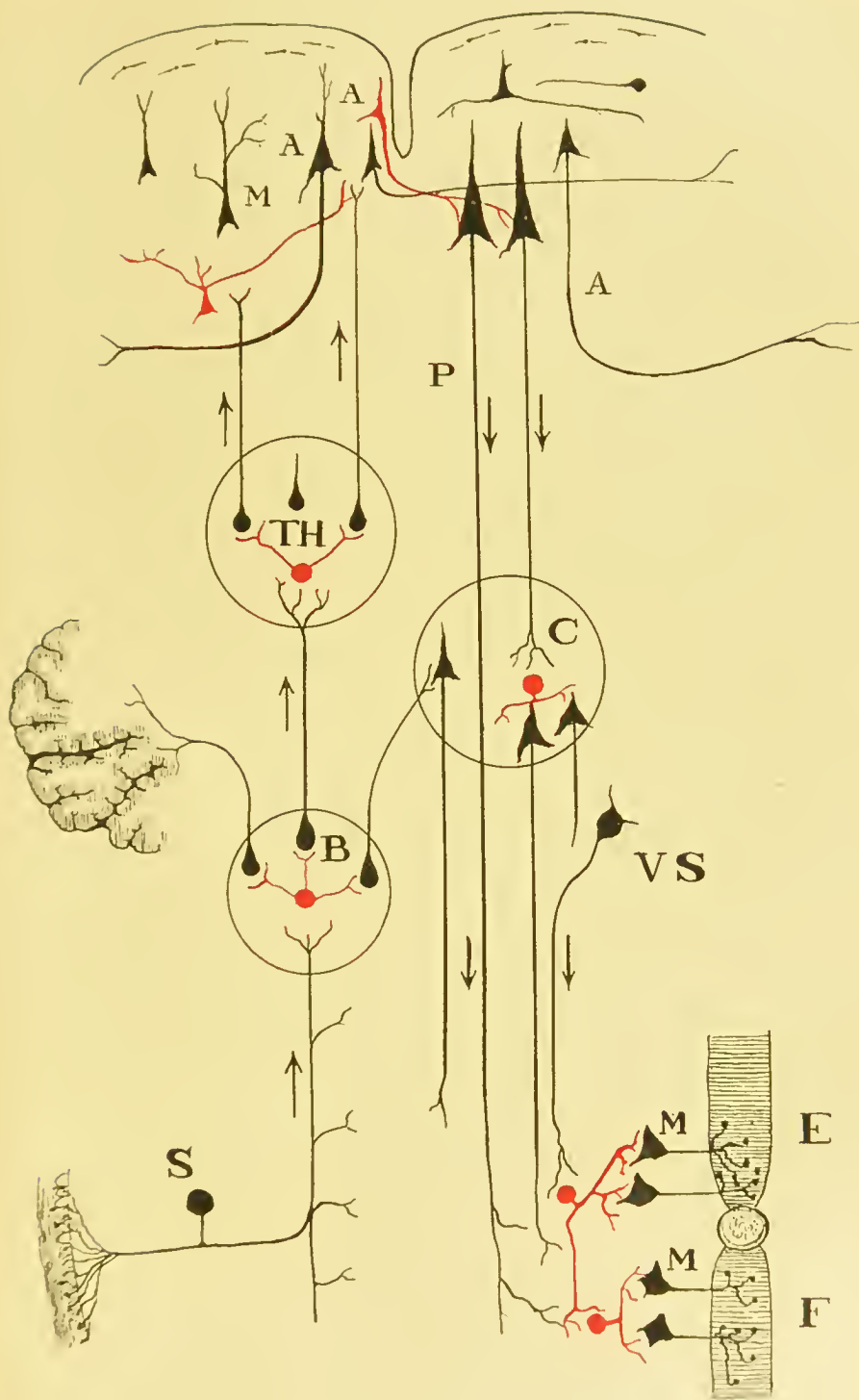
M = Motor neurons to E extensor muscles.

„ „ to F flexor muscles.

V.S = Vestibulo-spinal tract.

M' = Cells of Martinotti.

P = Pyramidal fibres arising from the Betz-cells of the motor area and proceeding without a relay to the grey matter at the base of the anterior horns.







flexor and extensor groups by  $a^1$ ,  $a^2$ ,  $a^3$  and  $b^1$ ,  $b^2$ ,  $b^3$ , the normal tonus at rest is equal between the two groups of muscles because the stimulus is equal, but if a stimulus which requires a flexor response excites the skin, there will be a rise of potential in  $a^1$ ,  $a^2$ ,  $a^3$ , and resistance will be diminished at the synapse; this will lead to a drainage of energy across from  $b^1$ ,  $b^2$ . Then there will be an augmentation of outflow of energy to the flexor muscles with contraction and a fall of energy in  $b^1$ ,  $b^2$ ,  $b^3$  with relaxation. By this means we see that the maximum effect can be produced with the least expenditure of energy. Whether these intercalary neurons exercise a special function of manufacturing this neurogenic substance is, like the drainage hypothesis, purely speculative.

**Degeneration arising from Transverse Lesions of the Spinal Cord as an Organ of Transmission.**—Transverse lesions of the spinal cord lead to degenerations of the afferent systems above the lesion. These degenerations will extend to the second neuron of the afferent path; in the case of the long fibres the degeneration will extend upwards as far as the nuclei of the posterior columns in the bulb, namely, the nucleus of the column of Goll and the nucleus of the column of Burdach. These systems of fibres respectively transmit kinaesthetic impulses from the lower limbs and trunk, the upper limbs, trunk, and neck. Besides these fibres with a long course there are fibres with a shorter course in the posterior column; they arborise around the cells of Clarke's column, which begins to appear at the second lumbar segment; therefore the fibres entering by roots at a lower level must run a certain distance upwards in the postero-external column before they arborise around the cells of Clarke's column. In the lateral columns the fibres which will degenerate upwards are the ventral and dorsal cerebellar tracts; these are situated at the periphery; the former consist mostly of crossed fibres, the latter of direct fibres; they are formed by the axons of the cells of Clarke's column.

Transverse lesions of the spinal cord in the cervical and upper dorsal regions cause degeneration of the descending cortico-spinal fibres in the direct and crossed pyramidal tracts, and also of the rubro-spinal and vestibulo-spinal tracts. The degeneration will be more pronounced in both antero-lateral columns than if the pyramidal fibres above were completely degenerated by destruction of the motor area or by a lesion of the pyramidal fibres in the internal capsule; moreover, the physiological effects, as we shall see, differ entirely. The importance of these tracts of fibres arising in the mesencephalon and the bulb is usually under-estimated.

We will now consider degeneration arising in the spinal cord of the proprio-spinal fibres which serve to associate or connect the nuclei of the spinal segments and the cranial nerve nuclei. These proprio-spinal fibres are both ascending and descending; they run in the posterior and antero-lateral columns, as a rule they are situated immediately around the grey matter, and are surrounded by the long afferent and efferent tracts of transmission already mentioned. They vary in length, but all

the segments are connected by means of these fibres, so that some extend the whole length of the cord. Consequently, in a transverse lesion a number of fibres will be found degenerated both above and below the lesion, no matter where the transverse lesion may be. Lesions, such as a myelitis, involving any extent of grey matter, necessarily cause a heavy degeneration of these proprio-spinal fibres, as well as destruction of the spinal motor neurons and the sensory terminals in the grey matter. Syringomyelia, causing destruction of the grey matter of the posterior horns, gives rise to loss of the sense of pain and of heat and cold, but not of touch and the kinaesthetic sense; it is therefore probable that Schiff was right in asserting that the grey matter was aesthesodie and the white matter of the posterior columns kinesodie.

With this brief introduction to the subject of the spinal cord as an organ of transmission and as an autonomic segmental organ, we can now consider it in connexion with reflex action as studied by the clinician and the physiologist.

**Reflex Action.**—The reflexes of the clinician are mono-muscular and may be divided into two great groups: (1) superficial cutaneous, and (2) deep or tendon reflexes. The former are plantar, cremasteric, and abdominal. When the skin is excited, the stimulus flows along the reflex arc to the motor neurons of the corresponding spinal segment, causing the muscle innervated by those neurons to contract. When a tendon—for example, that of the quadriceps—is put on the stretch and sharply tapped, the muscle contracts, provided the reflex arc is intact. Dr. Bastian, however, pointed out that in transverse lesions of the spinal cord caused by fracture high up in the cervical region, the knee-jerk is no longer obtained. Physiologists at one time were unable to explain this, and it was thought that Dr. Bastian was wrong in his view that the disappearance of the patellar tendon-jerk was due to the cutting off of cerebellar influence. We now know, however, that this explanation was really correct, and that those who maintained that it was due to damage to the grey matter far beyond the seat of the injury, namely, in the lumbar region, were wrong. The reflex arc can be proved to be intact in such cases by the persistence of the periosteal reflex, although the tendon-jerk is absent. The loss of the patellar tendon-jerk is due to the absence of the tonic influence normally conveyed by the rubro-spinal and vestibulo-spinal tracts, which are in intimate relation with the cerebellum by their connexions with the dentate nucleus.

In considering reflex action in the light of experimental physiology special attention must be given to the illuminating researches of Prof. Sherrington and Pawlow. Prof. Sherrington has shewn that the bulbo-spinal axis contains a number of complex pre-organised neuronie mechanisms of a reflex instinctive nature. Thus, the varied movements of the hind leg of the dog are effected by a complex sensory motor mechanism capable of many different purposive reflex actions necessary for the preservation of the individual and the species—for example, to scratch, to walk, to run, to gallop, to squat in defecation, to abduct or flex in

micturition. However, the same muscles enter into the effector and are innervated directly by the same spinal motor neurons, which accordingly form a *final common path* for a number of such reflexes. But these activities would be liable to confusion were it not for the special selective possibilities of receptors and the integrative co-ordinate adaptation necessary to fulfil a purposive action in response to a particular stimulus. Thus, the

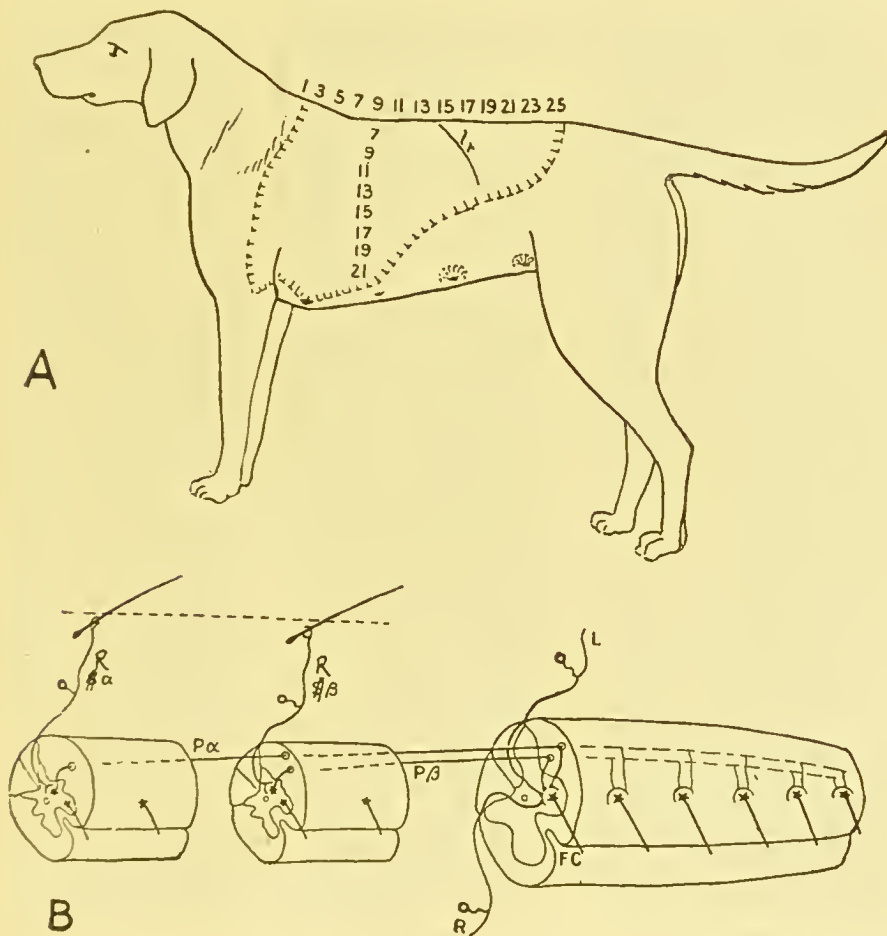


FIG. 56.—A, the "receptive field," as revealed after low cervical transection, a saddle-shaped area of dorsal skin, whence the scratch reflex of the left hind limb can be evoked; *lr* marks the position of the last rib. B, diagram of the spinal arcs involved. Receptive or afferent nerve-path from the left foot; *r*, receptive nerve-path from the opposite foot; *sa*, *sb*, receptive nerve-paths from hairs in the dorsal skin of the left side; *fc*, the final common path, in this case the motor neuron to a flexor muscle of the hip; *ra*, *rb*, proprio-spinal neurons. (Sherrington).

character of the reflex evoked depends upon the location of the stimulus, its quality and intensity, and to a limited extent on its duration. Prof. Sherrington's experiments, which will now be given, shew that the characters of a reflex may—as in the medusa and the beating heart—depend upon conditions of refractory phase. But they shew more: they locate, in the grey matter, the seat of the refractory phase and the path



by which the terminals of the afferent neurons of the reflex are associated with distant effector neurons which form the final common path for other reflexes.

The experiments are as follows: The spinal cord of a dog is transected in the neck region; the scratch or scalptor reflex in a few months' time becomes very easily elicited by appropriate stimulation in a certain defined large saddle-shaped area of skin indicated in the figure on page 245. It is interesting to note that the quality of the stimulus which may be applied to evoke the rhythmic alternate flexion and extension at hip, knee, and ankle, occurring at a frequency of about four times a second, is just such as would be produced by a flea biting or moving on the skin between the hairs, for Prof. Sherrington observes that the stimuli provocative of it are mechanical, such as tickling the skin or pulling lightly on the hairs. An electrical stimulus is most convenient for experimental purposes, but it must be applied in such a way as to stimulate the receptive nerve-endings which lie in the surface of the skin about the hairs. Consequently he adopted the following method of obtaining the appropriate stimulus to call forth the reflex. A broad, flat electrode is placed on any part of the body surface outside the saddle-shaped receptive area indicated in the figure; the other electrode consists of a fine gilt entomological pin so lightly inserted under the skin that its point lies among the hair-bulbs. If, however, it be pushed deeper, other reflexes may be produced and the scratch reflex inhibited. Clearly, then, the specialised receptor for this reflex is the superficial skin and the hair-bulbs with their nerve-endings. And the reflex maintains the same rhythm under the strongest stimuli as under the weak. These experiments shew the existence of a selective receptor in the area indicated, which transmits stimuli through the posterior roots of the spinal cord between  $sa$  and  $s\beta$ , but the motor spinal neurons which respond to the stimulus are situated in the anterior horn of the spinal cord far behind the region of grey matter into which the exciting impulses pass. Consequently there must be a connecting link between the grey matter at the two levels (*vide* B, Fig. 56). The scratch reflex is in a sense unilateral—stimulation of the left shoulder evokes the scratching action by the left leg; if the cord of the spinal dog (animal in which the cord has been previously transected in the cervical region) be semisectioned in the thoracic region so as to leave intact only the right lateral column, the scratch reflex can no longer be elicited by a stimulation of the left shoulder, whereas it can by stimulation of the right shoulder. The path of connexion, therefore, between receptor and effector lies in the lateral column of the same side. Prof. Sherrington speaks of this as a proprio-spinal path. He demonstrates its existence histologically by the following experiment: A transection of the spinal cord of the dog is made between the second and third thoracic segments; then there ensues a degeneration of all the fibres that enter the cord from the brain and the grey matter of the spinal cord above the lesion. If the dog be allowed to live a year, all the products of degeneration will have completely disappeared, and "a clean slate" below the lesion exists,



on which a new degeneration can be written. If, then, another transection be made between the fifth and sixth thoracic segments, the proprio-spinal descending fibres which have their cells of origin in the grey matter of the spinal cord between the first and second lesions—that is, in the third and fourth thoracic segments—degenerate and can be easily demonstrated by the Marchi method.

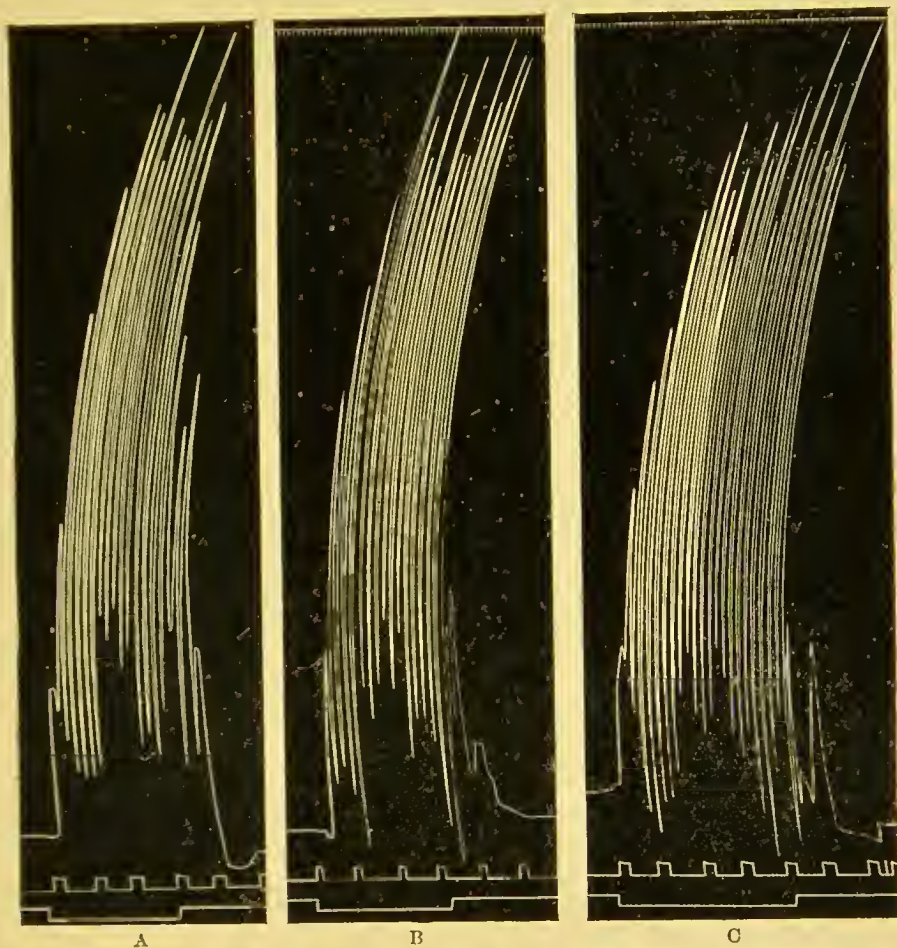


FIG. 57.—Tracings of the flexion of the hip in the "scratch reflex" of a "spinal dog. In A the reflex is evoked by lightly rubbing the skin at a point behind the shoulder, in B and C by unipolar faradisation, with weak double-induction shocks applied to the same point of skin through a needle-point lightly inserted among the hair-roots. Time marked in seconds below. At the top in B and C an electric signal marks the double-induction shocks delivered, and at the bottom an electric signal marks the time of application of the stimulation.

As shewn by the heavy degeneration, these proprio-spinal fibres are very numerous, and can be traced from the shoulder segments to the hind-limb segments. We have then by this method of successive degeneration clearly indicated that the afferent neurons of the shoulder region are linked up with efferent neurons of the hind-limb lumbo-sacral region, which neurons form a final common path to many reflexes of the hind

limb. The refractory phase, which, we have seen, is an essential condition for the scratch reflex, has its site in the central grey matter; it is a state of inhibition or rhythmical absence of passage of stimulus from afferent terminals to efferent discharge. It must be dependent upon alternate phases of conduction and non-conduction by this proprio-spinal path.

A very interesting comparison is made by the study of the extensor thrust or stepping reflex; this is elicited by mechanical stimuli applied to the plantar surface of the foot, and the response is followed by a relatively long refractory phase; it forms thus an important reflex mechanism of locomotion, providing much of the propulsive power; its repetition is required only at intervals considerably longer than the duration of the thrust itself, for after the thrust of the foot against the ground the limb has to execute a series of movements without touching the ground, in preparation for the next step, and this occupies a longer time than the thrust. It is reasonable to suppose that part of the means by which selective adaptation has secured this result is the evolution of the long refractory phase following the activity in the reflex arc of the extensor thrust.

One reflex seems to be precluded from acting on the motor neurons of the final common path when another and a different reflex is employing it. This is the result of a process of inhibition, the seat of which lies neither in the afferent neuron proper nor in the efferent neuron proper, but in an internuncial mechanism, synapse or neuron, between them.

There may be antagonism between reflexes employing the same final common path, and competition, as it were, between the excitatory stimulus used for the one reflex and the excitatory stimulus for the other. Thus, if while stimulation of the skin of the shoulder is evoking the scratch reflex the skin of the hind foot of the same side is appropriately stimulated, then a protective flexor-withdrawal reflex displaces the scratch reflex, and instead of alternate contraction and relaxation of the flexors the foot is drawn up by steady and maintained contraction of the flexors of the ankle, knee, and hip. These experiments teach us the important integrating functions of these spino-spinal (or proprio-spinal) fibres of the cord.

When an animal is deprived of the influence of the cerebrum upon the lower bulbo-spinal centres by section through the cerebral peduncles, it enters into a state of extensor decerebrate rigidity. When a decerebrate animal is suspended with its spine horizontal and its limbs pendent, the observer can note ten areas whence bulbo-spinal reflexes employing skeletal muscles can be obtained with facility. These areas are the soles, the palms, pinnae, the mouth, the snout, the tail, and cloacal region. Stimulation of any one of these areas causes a particular attitude, a reflex figure to be struck. These figures indicate a purposive action of withdrawal of the part stimulated combined with the attitude of running away. The stimulus affects one small part only of the skin, and the inflow of stimulus into the grey matter of two or three segments of the spinal cord

nevertheless produces alterations in the innervation-currents flowing to all the muscles of the head, trunk, and limbs, causing inhibition along certain tracts of neurons and impulsion along others. Here then exists an integrative action, which must depend upon proprio-spinal neurons linking up the grey matter of all the segments of the spinal cord, and bringing about a co-ordinate reflex action. The position of the limbs in the suspended animal in which decerebrate rigidity has been produced is that of slight active extension such as would exist if the animal stood on the ground. The museular tonus exerted against the force of gravity is in part due to impulses descending the cord, mainly of labyrinthine origin; and any attitude which is assumed by the decerebrate animal as a result of stimulus applied tends to remain—that is to say, a cataleptoid condition is produced. Prof. Sherrington has shewn, however, that if in such an animal the posterior roots supplying a limb be cut, the tonus in it is immediately lost; presumably, therefore, the labyrinthine impulses descending in the vestibulo-spinal tract tend to reinforce and maintain the discharge of innervation-currents along established lines of least resistance in the spinal reflex arcs, especially those concerned with gait and station.

In the stepping reflex there is alternately excitation and inhibition in the flexor neurons, whilst synchronously with that ensue alternately inhibition and excitation in the extensor neurons. These alternating reflex activities in flexors and extensors illustrate extremely well the principles of the reciprocal innervation of antagonistic muscles whereby co-ordinate purposive action can take place with the greatest efficiency and the least expenditure of neural energy. The destruction or decay of any of the systems of afferent, efferent, and association neurons, or the ascending and descending fibres of neurons of spinal transmission, must lead to inco-ordination by failure of that harmonious co-operation which has been gradually evolved in the upward development of the animal series, and the higher the order in the zoological scale the greater is the disturbance evoked by the degeneration of the fibres of the neurons of spinal transmission. The influence of the mesencephalo-spinal and the vestibulo-spinal fibres upon the spinal deep reflexes in man as compared with the lower animals is shewn by the facts stated on p. 248. Dr. Hughlings Jackson has followed Herbert Spencer in the view that cerebral impulses bring about successive actions, whilst cerebellar impulses effect continuous action. This generalisation is based upon clinical and experimental evidence.

*Experiments on Cortical Inhibition.*—Cerebral action is largely inhibitory on the lower spinal centres. Prof. Sherrington, by his experiments on innervation of the ocular muscles, has shewn that cortical stimulation produces both excitatory and inhibitory impulses. Also the experiments which he conducted with Hering on antagonistic muscles of the limbs demonstrated that the results of excitation of the cortex was the discharge of both inhibitory and excitatory impulses on the lower spinal centres by the pyramidal systems of fibres. Moreover, he has more recently shewn



that the results obtained on stimulation of the fibres in the internal capsule were as striking as those obtained from the cortex itself. It is therefore probable that the inhibitory effect produced by cortical stimulation is not in these cases due chiefly or even at all to interaction of cortical neurons on one another. The fact that it is much easier to get flexor movements from cortical stimulation than extensor movements, does not mean that this cortex is in touch with the flexors alone, and not with the extensors; it means that the usual effect of the cortex on these latter is inhibition. It does not mean that the extensors and the jaw-closers are unrepresented cortically, but that their normal representation in the cortex under the ordinary conditions of experiment has the form of inhibition, not of excitation; and this, unless specially sought, escapes observation.

After administration of strychnine or tetanus toxin, extension of the knee can be regularly excited from the cortex and from the very points of it that yielded flexion previously. Similarly when the face area of the monkey's cortex is tested by faradisation after exhibition of strychnine, the points of surface that previously yielded regularly the free opening of the jaw yield strong closure of the jaw instead. These experiments, moreover, give an insight into at least a part of the essential nature of the condition brought about by tetanus and strychnine poisoning. "These disorders work havoc with the co-ordinating mechanisms of the central nervous system, because in regard to certain groups of musculature, they change their reciprocal inhibitions normally assured by the central nervous mechanisms into excitations; the sufferer is subjected to a disorder of co-ordination which, though not necessarily of itself accompanied by physical pain, inflicts on the mind, which still remains clear, a disability inexpressibly distressing. Each attempt to execute certain muscular acts of vital importance, such as the taking of food, is defeated because from the attempt results an act exactly the opposite to that intended. The endeavour to open the jaw to take food or drink induces closure of the jaw, because the normal inhibition of the stronger set of muscles, the closing muscles, is by the agent converted into excitation of them." Prof. Sherrington considers that the virus of rabies may similarly upset reciprocal innervation, though its field of operation, at least in man, does not lie in the same group of mechanisms. He does not consider that these results are due to the action of these agents on the cortex itself, and he gives reasons and experiments shewing that the poison acts on the lower centres, spinal and bulbar.

The above-mentioned experiments throw a flood of light on the reflex functions of the bulbo-spinal structures and the mechanism of their integration. The afferent and efferent cortico-spinal systems of neurons are especially necessary for acquiring and perfecting new and refined tactile kinaesthetic modes of reacting to environment. The greater part of the cerebral cortex in man consists of association-neurons. Around the primary fissures, Sylvian, Rolandic, and calcarine, are the regions of the cortex in which the afferent projection-systems terminate and the



effluent motor systems start. These regions, according to Flechsig, only occupy one-third of the whole surface of cortical grey matter; the remainder consists of association centres. Myelination occurs at a later period in these association areas.

*Conditional Reflexes.*—Pawlow has shewn the important influence of psychical action upon organic functions and secretions. He found that the flow of the digestive juices is profoundly influenced by psychical impressions and by associative memory. Thus, if a cannula be placed in the duct of the submaxillary gland of a dog so that the rate of flow of saliva can be determined, it will be found that the animal always secretes a larger quantity of saliva when acid fluid is put in the mouth. This he terms an "unconditioned reflex," but if this fluid is coloured and shewn to the dog each time before it is put in the mouth, in a short time a conditioned reflex will be obtainable, for it will suffice to present the bottle of coloured fluid to the dog for increased flow to take place. Indeed, any stimulus entering the nervous system by any of the sensory avenues simultaneously with the "unconditioned reflex" may sooner or later lead to the establishment of a "conditioned reflex." Thus, the blowing of a horn in an adjoining room every time the acid fluid is put into the dog's mouth will set up such a condition of association in the central nervous system that the blast of the horn of itself will suffice to cause an increased flow. But if once the conditioned reflex has been effected, it cannot again be immediately obtained unless the unconditioned reflex has been previously effected. This may be interpreted as the establishment of an associative bio-rhythmical activity between the neurons of the sensory peripheral receptor and central receptor and the neural structures presiding over the lower unconditioned reflex. But when once the conditioned reflex has been fired off, this association is broken unless an interval of time be left, or it be re-established at once by establishment of the unconditioned reflex. These experiments in many ways correspond to what is observed in many habits of daily life; thus, washing the hands excites the desire to micturate.

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*THE AFFECTIVE TONE.*—"The organ of mind (highest centre) represents all parts of the body; in strictly equivalent words the highest centres are centres of universal co-ordination. It is thus that

they are the organ of will, reason, memory, and emotion, the four elements of mind or equivalents of consciousness" (Houghlings Jackson). In the study of the nervous system by neurologists, too exclusive an attention has been directed to the perceptual and intellectual functions of mind to the neglect of the affective side, and yet the study of nervous and mental diseases clearly shews the important part that the affective tone of the individual plays in all forms of disease, whether bodily or mental. The intellectual life is a graft on the affective life; it is of later development, and knowledge, as Ribot says, is not a master, as is usually considered, but a servant. For the affective life is the source and support of all the stable actions of the mind. The affective life depends upon the organic sensibility, which by ministering to the needs of the appetites and desires becomes the active although unconscious source of the great majority of our habitual actions. Organic sensibility is the source or foundation of all stable associations, individual and collective. Our appetites and desires determine the affective tone and upon this voluntary action is based. The affective tone of the individual depends upon the functions of the vasomotor and vagal nerves; it is continually oscillating about a mean point of equilibrium, a mental state that is neither pleasurable nor painful. Although neither pain nor pleasure can be said to constitute an emotion, yet one or other and sometimes both form an essential part of every emotion. We know little of the physiology of pleasure; it is a diffuse vague state of consciousness, clothed and enriched by perceptual and intellectual associated memories which we desire to experience again, and it forms an accompaniment of the healthy activity of bodily functions which does not exceed the ordinary normal powers of reparation that the organism possesses. The fundamental basis of the stimuli to this activity of bodily functions is the satisfaction of the desires, appetites, and instincts necessary for the preservation of the individual and the species. The preservation of the individual, however, depends not only on the maintenance of the nutritional equilibrium by the gratification of the appetites, but the body is protected from physical and chemical injury by pain and the unpleasant emotion of disgust. These are both states of consciousness which there is no desire to experience again, and when clothed and enriched by perceptual and intellectual memories, their causes can be avoided. Thus, by constantly furnishing the desire to prevent painful and injurious bodily conditions, they form even more than pleasure the basis of voluntary action. In the animal scale at first they form only psychical adjuncts to protective reflexes, but they come more and more to dominate instinctive reflex activities which only arise consecutively to injury. Besides physical pain many painful states may be related to the organic needs of hunger, thirst, the desire to breathe fresh air, the desire for sleep, for exercise and repose, for re-euperation after muscular fatigue, and, of especial importance, the desire to satisfy the sexual instincts. But besides these physiological cravings which play the dominant part in the conduct and habits of all human beings, there may be certain artificial cravings (induced by habit), for

example, for alcohol, morphine, cocaine, hashish, the discontinuance of the habit causing physical and mental pain. In fact the sentient being, whether animal or man, reveals a combination of appetites, of desires, of physical and psychical tendencies; and all those conditions, whether from internal or external causes which suppress or interfere with them, give rise to painful states, physical suffering, and mental pain.

Let us now consider the more simple physical pain, though even in this question there are still many points in physiology not definitely settled; for example, is there sufficient evidence to warrant us in accepting the existence of special nerves for pain, or is pain merely the result of injury by strong excitation of the nerves of general sensibility? It is known that pressure of a point of the skin by a bristle just short of the breaking-point causes pain. Heat of  $48^{\circ}$  C. causes a painful sensation; this is the temperature at which a neuroglobulin coagulates, causing changes in the nerve substance. The cornea, which is a delicate skin where the nerve-fibrils are almost naked, is extremely sensitive to slight irritation. Painful sensation depends, however, not only upon the intensity of the irritant, but also upon the irritability of the chains of neurons which form the sentient system of receptor, transmitter, and perceptor. This is a matter of common experience, especially in disease. The mental attitude of the individual plays a most important part in the subjective feeling and the objective manifestations of pain. Bichat said, "If you want to estimate the intensity of pain feel the pulse." Pain is felt in the cerebrum, and without the cerebral centres there would be no pain, only irritability and reflex discharge such as occur in a decerebrate animal. We remember physical pain by the perceptual concomitants that caused it or were associated with it. Whilst visual, auditory, tactile, gustatory, and olfactory impressions are referred to the external objects which produce them, the pains of pricking, cutting, or burning are not exteriorised into the needle, the knife, or the flame. Cutaneous sensibility to pain is therefore associated with the internal organic sensibility; it is precise enough as to localisation because in its prevention it is continually associated with perception of the special senses. The prevention of pain thus serves as a constant factor in the development of the special senses. The same cannot be said of pain affecting the internal organs, but according to a physiological law depending upon morphological conditions the mind refers the pain to a definite area of skin, and this pain is termed a "referred pain." Thus, in angina pectoris, in which there is irritation of the cardiac plexus, not only is there a state of precordial anguish, of constriction, of fear, and of a feeling as if the vital functions are about to be suspended, but pain which radiates down the inner side of the left arm occurs. This referred visceral pain can be explained by the fact that the afferent fibres of the cardiac branches of the sympathetic enter the same segments of the spinal cord as the sensory cutaneous nerves of the post-axial border of the upper limb, corresponding to the distribution of the ulnar nerve from the lowest cord of the brachial plexus. The viscero-vascular structures are supplied by the



fibres of the white and grey rami of the sympathetic, and strong irritation of internal visceral structures produces intense impulses which are carried by afferent visceral fibres into the grey matter of the various segmental metameres of the spinal cord; these by irradiation excite the neurons which receive painful stimuli from the associated skin-areas; the result is twofold, the establishment of a protective reflex by contraction of the correlative skeletal muscles and a painful sensation transmitted to the seat of consciousness, especially increased if this protective reflex is broken down voluntarily or involuntarily. Thus, pain has been defined by Prof. Sherrington as a psychological adjunct to a protective reflex. The mind is only cognisant by the senses of this particular painful stimulus coming from a definite skin-area; it therefore refers the pain to it. Thus the establishment of the protective reflex serves to keep the parts at rest; and the pain produced protects the internal organ by preventing that reflex being broken down voluntarily or involuntarily, for example, as in coughing in pleurisy. One of the trite sayings of Oliver Wendell Holmes was that "clergymen and persons without wisdom consider pain a mystery; it is a revelation"; and Richet is right in asserting that instead of considering pain as an evil, from a biological point of view, we ought to consider it the fundamental element of human progress; for as instinct is blind, intelligence is necessary to avoid pain. Moreover, pure automatic conduct is incapable of modifying actions according to the change of environment, because instinct does not foresee these changes. On the contrary, intelligence foresees and prevents pain in innumerable ways, whether arising from the non-gratification of the organic needs or from physical pain due to injuries which would damage the tissues and organs of the body. The more delicate the organ—for example, the eye and the ear—the more sensitive it is to pain. Again, the knowledge of things interests us, because it is a means of avoiding pain; suffering in others excites pity and the tender emotion, consequently pain plays a fundamental part in the intellectual, moral, and social development of humanity.

*Pain and its Conduction.*—Schiff taught that the grey matter is aesthesodic and the white matter kinesodic. Syringomyelia, in which the grey matter is destroyed and the white matter uninjured, is characterised by a condition of sensory dissociation. The patient feels tactile sensations, but no longer feels pain, or heat and cold. Prof. Sherrington has shewn that the impulse of painful impressions coming from one-half of the body leaves the grey matter and passes up the lateral column of both sides, rather more on the opposite. The painful stimulus is transmitted to the brain, but there is no certain evidence that pain is represented in any part of the cortex. Painful sensations, together with all afferent sensory stimuli, meet in the optic thalamus, the principal function of which is that of a sensory relay-station to the cortex. This mass of grey matter, including the external and internal geniculate bodies and pulvinar, sends afferent radiations to all parts of the cerebral cortex, but particularly to the projection centres about the primary fissures. It con-



tains two forms of cells, large cells like those of the anterior horn of the spinal cord and the motor area of the cortex, and smaller cells. The large cells are in all probability motor in function, and control the sub-conscious, involuntary, instinctive, automatic, mimic reflexes of gesture, physiognomical expression, and of primitive vocalisation. The evidence in favour of this is that experimental lesions in animals and spontaneous lesions in man invariably produce some degree of anaesthesia on the side opposite the lesion. Irritative lesions of the thalamus are frequently associated with severe pain in the opposite half of the body. It is well known, as was first pointed out by Sir Charles Bell, that in old cases of cortical hemiplegia the face on the affected side can only be imperfectly moved by the will, yet if the patient, under the influence of the emotions, laughs or cries, this side of the face is more strongly contracted than the non-paretic side. In lesions of the thalamus, on the other hand, the opposite is frequently observed. The patient, on the one hand, can voluntarily move the paretic side of the face well in all directions, as in shewing the teeth and voluntary laughing; on the other hand, in emotional expressional movements this side of the face is immovable. According to von Monakow, this condition is not met with in other cerebral lesions; therefore, although it does not occur in every lesion of the optic thalamus, yet the fact that it does not occur in any other cerebral lesion indicates that some part of the thalamus is associated with these reflex mimetic movements. Von Monakow, moreover, cites cases which seem to shew that it is possible "that secretory, vasomotor, and other tracts of fibres in connexion with the sympathetic nervous system have an abundant representation in the thalamus opticus."

But let us return to pain, and for the sake of argument say that pain is produced by a strong excitation transmitted by the grey matter and lateral columns of the spinal cord to the thalamus; here the feeling of pain is produced, but this is always associated with perceptual cortical feelings of localisation and cause, with secondary associations of time and space. If pain *per se* were represented in the cortex, then it should be continually revived in memory with the re-representation, but pain is forgotten as soon as it is over, and what we recollect are those intellectual perceptions which will enable us to avoid it in the future. Stimulation of the cortex of the central convolutions has been performed without anaesthesia in man (Dana); the only effect was a slight numbness and tingling in the extremities, fingers, thumb, etc., not amounting to pain. The brain can be cut without causing pain; in animals stimulation of the thalami, in contradistinction to the cortex, gives rise to the manifestations of pain. Pain is unknown as an aura in cortical epilepsy, and no region of the cortex has been proved beyond doubt to be associated with pain, although it has been asserted that the gyrus fornicatus is a centre for pain.

Prof. Sherrington has shewn that in a "spinal" animal the pain reflex is prepotent. Take, for example, the reflexes which engage all the muscles of the hind limb in purposive movements of a useful character; if a

reflex, such as scratching, is set up in the right leg to remove a stimulus resembling a parasite among the hairs of the front of the body, and, while this scratching is proceeding, a painful stimulus (like a thorn) is applied to the pad of the left foot, a flexor withdrawal occurs, accompanied by a replacement of the right foot on the ground to act as a support. Experiments shew that the sexual reflex in the lower animals—for example, frogs and tortoises—is even more potent than pain reflexes, and Prof. Sherrington rightly affirms “that reflexes arising in the species of receptors which, considered as sense organs, provoke strongly affective sensations, *ceteris paribus*, prevail over reflexes of other species when in competition with them for the use of the final common path.”

If now we examine the effects of painful stimulation of the skin in a decerebrate animal, in which therefore a wider conjunction of reflex arcs is left than in the spinal animal, a number of reflexes are obtained which Prof. Sherrington terms “pseudo-affective,” because the neural mechanism for the perception of pain is cut off from its connexion with the receptor; but it is still in connexion with a purposive instinctive reflex motor mechanism of offence and defence, the action of which is usually considered as the outward expression of the inward affective feeling, and it may be assumed that had the brain been present the feeling would have occurred. Such a decerebrate animal, when the sciatic nerve is stimulated, exhibits movements indicative of offence and defence, forward cyclic movements, as in progression, turning of the head toward the part excited, opening the mouth, retraction of the lips, movements of the jaw as in snapping, movements of vibrissae, lowering of the head, dilatation of the pupils, vocalisation angry in tone (sometimes plaintive, sometimes snarling), and with these a passing increase of arterial blood-pressure. These movements are ineffective and of brief duration, possibly because they are deprived of the perceptual reinforcement which the brain gives. Prof. Sherrington proceeded to ascertain how these pain reflexes can be abolished in order to establish the probable path of pain reflexes in the cord. The method Woodward and he adopted was to compare by means of the above reaction the effect of two stimuli symmetrically but successively applied on opposite sides of the body after a semisection of the spinal cord or other lesion of the spinal cord headward of the nerve path stimulated. He concludes that each lateral column conveys impulses from both halves of the body, and somewhat preponderantly from the crossed half; and this is true for these arcs, whether they be traced from skin, muscles, or viscera.

Goltz, by a series of careful and judiciously planned experiments, was able to remove the whole of the cerebral hemispheres and a large part of the basal ganglia from a dog in successive operations, and the animal by patient and careful feeding was kept alive many months, and valuable observations on the decerebrate animal were made. Its behaviour, as compared with his own normal dog, is a most valuable psycho-physiological study, and I will briefly describe the more important features of this comparison. The animal would lie curled up

like a normal dog, it could be aroused by the loud blowing of a horn, and by blowing through a tube a current of air on to its skin, when it would raise itself on its four legs and shake itself. If the animal had been roused by the blast of the horn it would put its paw up to its ear as if something unpleasant had happened. When the animal was removed from the pen, as it was every day, to be fed, it growled, snapped, and snarled like an angry brute, and resisted and struggled to be free and return to its cage; it shewed, in fact, exactly the same signs of anger as the decerebrate dog whose sciatic nerve was stimulated in Sherrington's experiment—lowering of the head, bristling of the hair, retraction of the ears, and growling, biting, and snapping. Although removal from the cage every day meant to the animal appeasement of hunger, yet this animal every day for eighteen months, until the day of its death under chloroform, gave the same instinctive signs of anger, and never joy, fear, or affection. Goltz compared the behaviour of this animal with the behaviour of his own animal, who would allow him to pull his tail and tread on his foot, shewing, however, by his expression that he felt it painful, but he tolerated it and controlled his feelings because of affection for his master. The decerebrate bitch, on the contrary, made no distinction between the stranger and the man who had fed her every day. She had no memory, but still possessed desires and instinctive reactions. When hungry especially, like the wild animals in the Zoological Gardens, she performed continuous pacing movements of locomotion in one direction from right to left, or the contrary; moreover, she would place her two forepaws on the front of the cage, standing on her hind legs. She could maintain her position on the four limbs on a smooth and sloping surface, and defecated and urinated like a normal bitch. The expression of the dog was entirely devoid of intelligence, and it did not wag its tail, nor did it ever shew signs while asleep of dreaming like other dogs. When fed, the food was placed near its muzzle; it then masticated and swallowed it like a normal dog. An interesting experiment was made by Goltz in relation to the emotion of disgust. Pieces of meat were soaked in a solution of quinine and given to the animal; it refused to eat the meat. The same pieces were given to the normal dog; it wagged its tail, pulled a face, and looked to its master as much as to say, "Well, this is unkind of you to give me this! I don't like it, but to oblige you I will swallow it," which he did upon encouragement. Not even hunger would make the dog without a brain swallow the bitter meat. Now this interesting fact supports Richet's view that bitter and acrid substances which are unpleasant are as a general rule poisonous or noxious, whereas sweet-tasting things for which we have a gust (*goût*) are pleasant and beneficial. So that disgust (*dégoût*) is protective to the alimentary canal and the vital bodily organs, just as pain protects the external surface of the body. This animal ceased to have oestral periods and never shewed the slightest sexual desire. The animal was deprived, however, not only of the cerebral cortex, but also of the basal ganglia, the corpus striatum and optic thalamus. How it would have



behaved had it been possible to destroy the cortex leaving these structures we do not know, but the experiments of Nothnagel, Bechterew, and many others rather indicate that these structures are very important in relation to the emotions. Pagano has published a number of experiments on adult and new-born dogs, which I will briefly relate, although I am of opinion that the experiment of injecting fluids such as curare into the basal ganglia, even although controlled by simultaneous coloration by a dye so that the extent of the effect of the irritant can be gauged on post-mortem examination, is not altogether trustworthy. This experimenter states that he has shewn that excitation of the caudate nucleus and of the optic thalamus provokes in adult dogs movements of expression distinctly attributable to determined emotional states, accompanied by visceral phenomena. It was, however, important to demonstrate that there was a real functional autonomy; he therefore excited the caudate nucleus in new-born animals. From his experiments he concludes that in the basal ganglia are found at birth physiological pre-organised mechanisms of emotional reactions. The cerebral cortex not being functional at birth is, therefore, not indispensable for these emotions. He concludes also that the superior psychical centres which are superimposed on the lower centres are only a new source of stimulus for primordial expression, but at the same time the origin of secondary modifications of emotional expressions. His experiments consisted in injecting 0.1 c.c. of a 2 per cent solution of curare coloured with thionin into various portions of the caudate nucleus. The results obtained are as follows: Excitation of the anterior third and of the middle third of the caudate nucleus, especially in their inner half, provokes the emotional phenomena of fear. They are characterised by the attitude of the body, the physiognomy, the cardiac, respiratory, intestinal, and vesical phenomena, the state of the pupils, and the menacing noises which exaggerate considerably these manifestations of terror. Excitation of the anterior extremity of the caudate nucleus produces phenomena of psycho-motor agitation of the same kind, and expresses a mingling of the two emotions fear and anger. Excitation of the posterior portion provokes manifestations of anger. Excitation of the anterior third produces erection of the penis almost as strongly as stimulation of the lumbar centre.

Prof. Sherrington has performed some notable experiments which shew that an animal, whose brain has been cut off from its connexion with the heart and viscera generally, still exhibits joy and sorrow, anger and fear, disgust, and sexual instinct. He divided the spinal cord in a dog in the lower cervical region, and when the animal had sufficiently recovered from the effects of the operation he cut both pneumogastric nerves. In this way the brain was cut off from any afferent impressions from the viscera, yet the animal shewed joy at seeing the attendant who fed him, anger at a stranger, and fear and sorrow when scolded. One animal only nine weeks old, kennel-fed, was thus operated upon, and when given milk in which pieces of dog's flesh had been placed absolutely refused to touch this flesh in any circumstances, and shewed marked signs of



disgust. Prof. Sherrington lays particular stress on this experiment as proving that even the primitive emotions appear to involve perception, and seem little other than sense perceptions richly suffused with affective tone. Of course, Prof. Sherrington is aware that these experiments are not conclusive, for although the animals may have expressed emotion in their facial expression and attitude appropriate to the exciting cause, although the viscero-vascular and much of the muscular expression was cut off from the sensorium, yet we have no means of knowing the subjective feeling of the animal, and "a small but notable fraction of the latter, namely, the facial, still remained open to react in the centres with which consciousness is colligate." Again, Lloyd Morgan, in connexion with this experiment, states: "The avenues of connexion were (only) closed after the motor and visceral effects had played their part in the genesis of the emotion, on the hypothesis that the emotion is thus generated. Although new presentative data of this type were thus excluded, their representative after-effects were not thus excluded." In reply to this criticism Prof. Sherrington remarks: "But it is noteworthy that one of the dogs under observation had been thus experimented upon when only nine weeks old. Disgust for dog's flesh could hardly arise from the experience of nine weeks of puppyhood in the kennel." Now this aversion to dog's flesh was due to olfactory impressions, and that "dog will not eat dog" may, in the long procession of the ages, have led to the establishment of a pre-organised mechanism by which disgust at dog's flesh might occur reflexly in the medulla: the paths of smell and taste were still open, and the only means the dog had of shewing the aversion it exhibited. We see that Goltz's dog exhibited disgust at meat soaked in quinine, although the gustatory cortical centres could not have been acting.

New-born animals are excited to the complex act of sucking and pressing forward the forelimbs, and it is said that the stimulus is smell, for such are not performed if the olfactory nerves of the puppy are destroyed. Moreover, anencephalous monsters cry and shew signs of pain and desire for food, and they are capable of the complex acts of sucking and crying without any cerebrum. There must, therefore, be a pre-organised mechanism for crying and sucking in the base of the brain. In mammals the lips and the muscles of the lips have been primarily developed for the purpose of sucking, the nostrils and the muscles that act on the nostrils for the purpose of breathing during the act of sucking. The senses of the young mammal require to be educated in order to be able to adapt itself to its environment, consequently it is for a time helpless and dependent upon its mother for nutrition and protection; thereby has been evolved a pre-organised nervous mechanism for crying which involves the integration of even a larger number of neurons than the act of sucking.

In the normal and quiescent non-emotional state an equable reflex tonus by afferent stimuli is maintained in somatic, respiratory, and viscero-vascular muscle, but under the influence of emotion (rage) there

is a surcharge of nerve potential flowing out through the somatic and respiratory systems of neurons, consequently there may be a drainage away of the normal flow of potential by the viscerovascular neurons, and a vascular dilatation will occur; or the vascular dilatation may be explained by antidromic discharge along the posterior roots, which may, as Dr. Bayliss's experiments prove, lead to vaso-dilatation (p. 80). But how are we conscious of this change in our bodily state? By the afferent impressions to the brain from the skin, muscles, and viscera, but mainly the two former, and these impressions will arise in the whole column of sensory cells, somatic and visceral, from the top of the fifth nucleus to the end of the spinal cord. Before reaching the seat of consciousness, however, these impressions will all be projected into the thalamic grey matter, where a fresh relay of neurons occur. But the thalamic region is also a station for receiving impressions from the special senses—hearing, sight, touch, taste, and smell—where relay-neurons occur by which the several special-sense stimuli are conveyed to definite regions of the perceptive cerebral cortex. *The thalamus may thus be the great subconscious centre for the elaboration, integration, and co-ordination of sensory impressions derived from organic changes in the body and those brought by the special senses from the material world around.* The thalamus is connected with the corpus striatum, and it is possible that both the basal ganglia may be primary centres of emotional discharge to the lower centres.

Every thought tends to activation, and thoughts based upon the revival of memories of past experiences are more or less suffused with affective tone, according to the nature of the experience and the temperament of the individual. There will thus be a tendency to revival of the physical concomitants (emotions) of that affective tone. It does not require a delicate instrument to prove the truth of this statement in many instances, for we know that the recollection (revival in consciousness) of a great sorrow or injustice will awaken sometimes a more violent emotional discharge than actually occurred at the time it was experienced. The experiments of Féré, Tarchanoff, Veraguth, and Jung and Petersen tend to support this conclusion; these observers have shewn that if the body of an individual is introduced into the circuit of a galvanometer through which a weak current is passing, and the resistance is so arranged by means of a rheostat as to enable them to bring the needle to zero on the scale, psychical conditions will lead to a deflection of the needle of the galvanometer. The inference is that the psychical change produces some physical change by which the current passes less readily or more readily through the body.

The results previously obtained by Féré and Tarchanoff have been corroborated and further elaborated by Veraguth, who found that if an individual introduced into the circuit be read to, deviation of the mirror is noted when passages associated with emotional tone are reached. Or if a series of unrelated words is pronounced by him, the words connected with some emotional complex produce an effect on the galvanometer, whilst indifferent words have no effect. He is unable to explain the

changes in resistance. Jung and Petersen, who have repeated and elaborated the above experiments and applied the method of investigation to cases of dementia precox, conclude that the change in resistance is due to the relative condition of secretory activity in the sweat-glands.

A perception or an idea arises ; it may suddenly, and before it can be controlled by the higher centres, lead to a diffuse emotional discharge,—that is, a stimulus irradiates downwards into lower centres before it can be controlled. But when a person is of a stable temperament and has habitually practised control, the tendency of the perception or idea is to irradiate into the higher association-centres, resulting in deliberation, judgment, and inhibition of the emotions. Perhaps the tendency at the present time is to suppress the affective side of our nature too much. "It should be the aim of mental culture to retain the emotions within the sphere of intellectual life, and so get the benefit in the supply of interest and energy required for effective volition. Disordered emotion may act upon the animal life, the organic life, and the intellectual life. It may grave itself in the lineaments of the countenance, or declare itself in the habit of the body ; it may initiate or aggravate organic disease, producing, according to its duration, a transient or lasting derangement, and it may temporarily obscure or permanently vitiate the intelligence." (Maudsley.)

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NEUROGLIA.—The supporting tissue of the nervous system which must now be considered is the neuroglia. It has already been pointed out that the neurilemmal cells forming the primitive sheath of Schwann of the peripheral nerve-fibres may be developed from the ganglion-crest, and therefore be of epiblastic origin like the connective-tissue cells of the central nervous system. In both instances we know that when degeneration occurs those cells which serve as the supporting scaffold of the neurons undergo proliferation. There is no doubt that the neurilemmal cells are phagocytic ; Dr. Bevan Lewis long ago pointed out that the neuroglial cells of the central nervous system also exercise a phagocytic action, and many recent observers, including Nissl and Marinesco, are of the same opinion. Before, however, discussing the function of the neuroglial cells, and the conditions which determine their proliferation and formative hyperplasia, it is desirable to describe the morphological appearances of these cells when appropriately stained.

There are several methods of staining which are useful to display the structure of the neuroglia. By the fibril-silver method of Cajal the

FIG. 58.

Phases in the development of neuroglial cells and fibrils (Watson). The drawings are all from cells of the cortex cerebri, stained by the Heidenhain erythrosin method. They appear somewhat diagrammatic, partly from being drawn in one plane, partly from the process of reproduction, but are little more so than the preparations shew. The parts shaded grey were stained pink in the specimens.

Fig. 1, a and b.—Dividing neuroglial nuclei surrounded by an indefinite amount of protoplasm.

Fig. 2, a and b.—Protoplasmic processes more definitely formed.

Fig. 3, a and b.—Commencing condensation of protoplasmic processes producing darkly staining fibrils.

Fig. 4, a, b, c.—Mode of attachment of the processes to a vessel-wall. In a and b there is apparent partial differentiation of the protoplasm of the "feet" into fibrils.

Fig. 5, a and b.—Further development of fibrils. The nucleus is more darkly stained, and in b the pink-stained protoplasm somewhat less in amount; a, shews a "recurved," and b, "bifurcated" fibrils.

Fig. 6.—The protoplasm is almost entirely differentiated into fibrils, and the nucleus is shrunken and stains darkly.

Magnification, 1000 diameters.





Fig. 1.



Fig. 2.



Fig. 3 a.

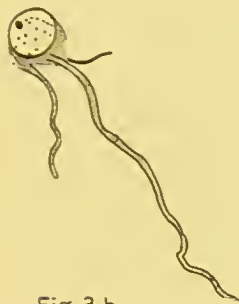


Fig. 3 b.



Fig. 4 a.

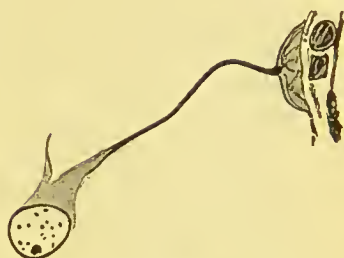


Fig. 4 b.

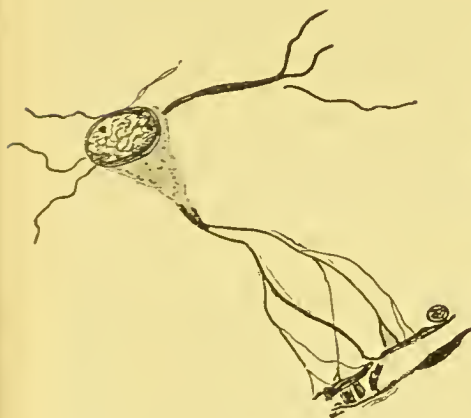


Fig. 4 c.



Fig. 5 a.



Fig. 5 b.

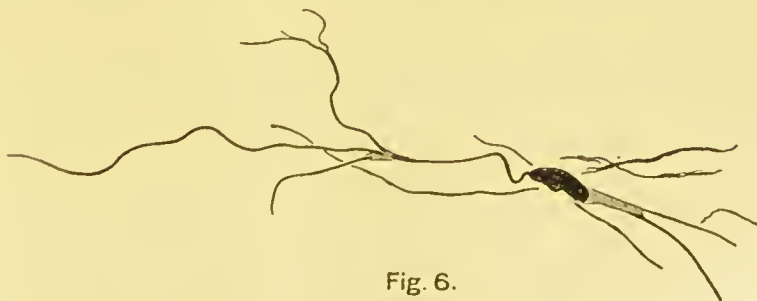


Fig. 6.

neuroglial cells are extremely well shewn ; they are also seen by the other silver methods of Cajal and Golgi, but the advantage of the fibril method is that the nuclear structure is differentiated from the cytoplasm by the stain. Van Gieson's method also demonstrates the neuroglial structure remarkably well. The Weigert glia method is very useful for shewing only the glial fibrils, but it is somewhat difficult to obtain successful preparations. The method, however, which I find the best is the Heidenhain iron-method counter-stained with eosin. When this process is employed the structure of the separate neuroglial cells and the mode of their proliferation and hyperplasia are readily discernible in sections of the central nervous system. I cannot do better than reproduce the Fig. (58) which illustrates a paper by my late assistant, Dr. G. Watson, on "The Histology of Juvenile General Paralysis." The nuclear membrane, the contained nucleoli and chromidian granules are stained deep blue and the cytoplasm pink ; the branching processes of the cells in a more advanced state of development are stained deep purple. All phases in the development of these neuroglial cells can be observed in chronic inflammatory conditions, also in degenerative processes of the central nervous system.

The neuroglial cells may for no known reason take on an active formative proliferation in the central nervous system leading to the formation of a gliomatous tumour. The glial cells proliferate rapidly and infiltrate the nervous substance, pushing aside and even destroying the neural elements. An increased amount of embryonic tissue in the form of neuroglia may persist around the central canal of the spinal cord ; with this there is an increase of thin-walled vessels which are liable to rupture, the effused blood causing a destruction and hollowing out of the adjacent grey matter with corresponding loss of function. (*Vide* Art. "Syringomyelia.")

Weigert in 1890 formulated the following important law regarding the neuroglia. When, from whatever cause, nervous tissue disappears, the neuroglia always reacts by a nuclear and fibrillar proliferation. Nissl in 1894 developed a similar idea, saying—when a nerve-cell directly attacked by a noxious agent undergoes a regressive transformation, the surrounding neuroglial cells present a progressive transformation. (*Vide* Plates II. III.).

Then Stroebe, Nissl, Lugaro, Cajal, and Marinesco shewed that neuroglial cells may be seen surrounding the nerve-cells of the cortex in the normal state. In secondary degenerations the neuroglial tissue proliferates and takes the place of the nerve-fibres, giving rise to a condition termed *sclerosis*. The Weigert and Weigert-Pal methods of staining are employed now instead of the old carmine method for displaying the secondary degenerative sclerosis of systems and tracts in the central nervous system. On the supposition that the sclerosis was primarily the cause of the disease and not secondary to decay and death of the neurons, many nervous diseases were labelled sclerosis. Thus, *tabes dorsalis* was termed posterior spinal sclerosis ; again, the name

idiopathic lateral sclerosis is a relic of the once prevalent view that a primary sclerosis of the lateral columns was a pathological entity. In disseminated sclerosis, tracts and islets of nerve-fibres are gradually replaced by dense neuroglial tissue, especially fibrils; this, however, is secondary to destruction and absorption, first of the myelin sheath and later of the axons; the pathology of this disease is unknown, but it might be explained by the slow, limited, and localised action of some lipolytic ferment which attacks the myelin covering of the nerve-fibres. According to Nissl the neuroglia plays an important part in the destruction of the nerve-cells, the neuroglial cells becoming more apparent in pathological processes and absorbing the products of degeneration of the nerve-cells. The fine granular corpuscles seen in the cortex are really neuroglial cells; there are no leucocytes in the cortex except in the case of abscess. Marinesco agrees with Nissl, and considers that the neuroglial cells have a phagocytic function, and he terms it *neuronophagy*. Ossokine maintains that the neuronophagy should be considered a secondary phenomenon occurring only as a result of profound modifications of the nerve-cells. Alzheimer recognised that in certain circumstances the neuroglial cells may contain in their interior granulations and detritus of very different nature and origin, but he does not consider that it has been demonstrated that the group of proliferated neuroglial cells existing around and even in the interior of nerve-cells can possess a phagocytic function. They would rather serve to refill the place left free by the destruction of the nerve-cell. He remarks that there are a certain number of lesions of nerve-cells unaccompanied by proliferation of satellite cells. With this opinion I agree. Some authorities believe that a symbiosis exists between the nerve-cells and the satellite cells. From my observations I should be inclined to explain the proliferation of the satellite cells which is seen in acute toxic conditions as due to the failure of assimilative metabolic processes in the nerve-cells as a result of the poison, consequently there is more nutriment at the disposal of the satellite cells, and they are stimulated thereby to proliferation.

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**THE CEREBROSPINAL FLUID.**—How are the neurons of the central nervous system nourished? in other words, what is the ambient medium? Dr. L. Hill concludes that the cerebrospinal fluid is the ambient medium. Although there are lymphatics in the adventitia of the vessels of the central nervous system there are no lymphatic glands, and these lymphatics cannot serve as a medium of gaseous and metabolic exchange between the neural elements and the blood in the capillaries in the same way as in the rest of the body.

A full consideration of the cerebrospinal fluid is necessary to enable the reader to understand the nature of many pathological processes occurring in the central nervous system; moreover, the withdrawal of a small quantity of cerebrospinal fluid during life and its subsequent examination by microscopical, bacteriological, chemical, and bio-chemical methods have in recent years proved most valuable in diagnosing many important diseases of the nervous system.

**The Cerebrospinal Fluid in Relation to Diseases of the Nervous System.**—The study of the cerebrospinal fluid is of relatively recent date. After Cotugno, who discovered it in 1784, the names of Magendie (1825-42) and Quincke (1890) are especially associated with our knowledge of its composition and functions. All physiologists are agreed that its chemical and physical properties are different from those of any other fluid in the organism.

*Chemical and Physical Properties.*—The normal fluid is clear, like water. It has a specific gravity of 1.006, a slightly alkaline reaction, and is devoid of all corpuscular elements; it contains traces only of albumin, becoming very slightly cloudy on heating. The principal constituent is sodium chloride, but it contains traces of carbonates, phosphates, and urea, and also a reducing substance which has been proved to consist of dextrose. The average amount of cerebrospinal fluid is 120 to 150 c.c. It varies in amount in pathological states, being increased when the volume of the brain is diminished, and vice versa. In general paralysis it may be enormously increased. Cerebrospinal fluid is a fluid *sui generis*. Although it resembles blood-plasma and lymph in the nature and amount of its inorganic constituents, the only protein matter which is present is a globulin; true albumin is absent. This and the absence of fibrinogen are marked differences between it and exudations from the blood. In other words, it is not a simple exudation, but a true secretion. There is a difference of opinion as to the site of its secretion, but most authorities attribute the function to the choroid plexus. The cerebrospinal fluid, formed in the ventricles of the brain, normally escapes continually through the foramen of Magendie at the apex of the fourth ventricle and along the glossopharyngeal nerves into the subarachnoid space. It passes from the cranium to the spinal canal at each cardiac systole; this fact, discovered by Magendie, has been demonstrated by François-Franck, by inserting a flag into the subarachnoid space through the atlanto-occipital ligament, and noticing the downward movement.



*Source, Destination, and Functions.*—Willis in 1664 called attention to the glandular nature of certain reddish granulations, and most people have accepted this view of the function of the choroid plexus. Pettit and Girard's experiments and histological observations demonstrated the secretory functions of the epithelium which covers the choroid plexus of the lateral ventricles. If we can accept these observations as conclusive, we need no longer consider the ependyma of the ventricles, the vessels of the pia mater, and the choroidal vessels, apart from their covering epithelium, as the source of this fluid (see Fig. 59). If the choroid plexus



FIG. 59.—Drawing from a photomicrograph of cells of the choroid plexus (human) stained with methyl blue and erythrosin. The cytoplasm contains a number of round and oval clear areas, probably due to the contained secretion. The appearances closely resemble those met with in the cells of the lacrimal gland. Magnification, 1000 diameters.

is continually secreting this fluid, we can understand its unique chemical composition and its freedom under normal conditions from all corpuscular elements. There is abundant evidence that this fluid is continually being secreted; for Mathieu has collected a number of cases in which large quantities of cerebrospinal fluid have drained away daily in consequence of injuries of the subarachnoid space by which a communication was established with the exterior. Surgeons have often recorded observations on patients who, after fractures of the base of the cranium or extirpation of sub-basilar polypi, have lost large quantities of fluid, amounting in the twenty-four hours, in some few cases, to between one and two litres (Billroth, Verneuil, Routier, Tillaux). Cases, also, have been recorded of daily

dripping of large quantities of cerebrospinal fluid from the nose (Halliburton, L. Hill, and St. Clair Thomson).

If there is a continual flow of the cerebrospinal fluid, where is its ultimate destination, and what are its functions? We know perfectly well that a large quantity of cerebrospinal fluid can be drawn off by lumbar puncture, and that the pressure with which it flows out of the cannula is in proportion to the pressure in the closed cavity which contains it. It cannot be continually secreted and not flow away. According to one view, it escapes along the lymphatics of all the cranial and spinal nerves, thus reaching the receptaculum chyli and thoracic duct, passing through the paravertebral lymphatic glands in its passage, and eventually returning, therefore, to the venous circulation.

Flatau's experiments by injection in the rabbit (via the olfactory nerve in particular) demonstrate that the fluid follows the course of the perineural sheath, then passes directly into the lymphatic networks of the nasal mucosa, thence it arrives at the glands of the neck and the naso-pharyngeal cavity; but the injection never runs to the surface of the mucosa, as Retzius asserted. Some of the cerebrospinal fluid may, and probably does, escape along these perineural lymphatics, and it is possible that these are the avenues of infection in the production of tuberculous, syphilitic, epidemic, and pneumococcic meningitis. However, the observations of Cushing favour the view that the fluid contained in the cerebral subarachnoid space and perivascular canalicular systems finds its exit from the cranium by opening into the longitudinal sinus. Cushing states that, after the intracranial pressure is raised by injection of normal saline solution, the fluid does not escape readily from the subarachnoid cavity; even under pressure not more than 60 to 100 c.c. escapes in half an hour perhaps. He agrees with Adamkiewicz that there exists a free communication between the subarachnoid space and the longitudinal sinus. He questions the correctness of Key and Retzius's hypothesis that the Pacchionian glands act as a filter, for, as he justly remarks, they do not exist in young people or in the lower animals. The nature of these openings of the subarachnoid space is not known, but probably they run obliquely forwards, like the veins, into the sinus, and have, like them, a valvular action, so that fluid can flow into the sinus, but blood cannot flow back. He could inject the subarachnoid cavity and the longitudinal sinus, but very exceptionally in the converse direction. Mercury injected into the subarachnoid cavity found its way into the sinuses, jugular veins, and right heart. A non-absorbable gas introduced into the subarachnoid space produced death by cardiac air-embolism, and if the jugulars were exposed, bubbles of it could be seen pouring down towards the heart. Exposure of the cervical lymphatics and of the thoracic duct, on the other hand, shewed in all instances a complete freedom from gas.

There is every reason, then, to believe that a quantity of cerebrospinal fluid is constantly being secreted, and that it fills up all spaces, cracks, and crevices in the subarachnoid space and its annexes, a quantity

proportional to the amount secreted continually escaping. The pressure on the whole cerebrospinal axis is thus uniformly maintained; but where the vessels of the pia-arachnoid run in the sulci or dip into the substance of the brain, the layer of the pia mater follows like a sleeve, forming thus a canalicular system in the nervous substance and containing cerebrospinal fluid. This canalicular system is called the perivascular lymphatic system: it does not contain ordinary lymph, but the cerebrospinal fluid, which apparently plays the part of the lymph of the central nervous system. The vessels of the brain have comparatively thin walls, and the arteries relatively few muscular fibres and vasomotor nerves. The

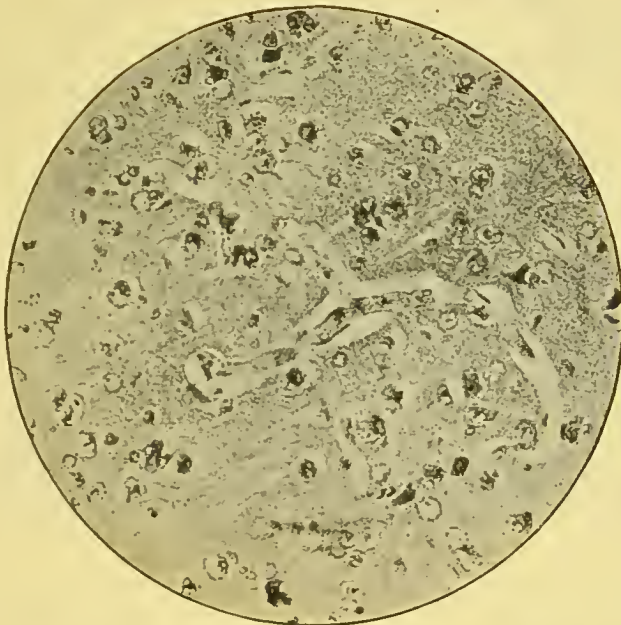


FIG. 60.—Photomicrograph of the cortex cerebri of a *Macacus rhesus* in which Dr. L. Hill had produced experimental anaemia by ligation of two carotid arteries and one vertebral artery. The canalicular perivascular system is well exhibited by clear spaces around the empty vessels. The perivascular spaces are seen to be connected with the perineuronic spaces; this is rendered clear by the empty condition of the small blood-vessels. Magnification, 250 diameters.

uniform pressure of the fluid sleeve which surrounds them supports the column of blood. The whole central nervous system being contained in a closed space, the cerebrospinal fluid fills up all the space which is not occupied by tissues or blood, and serves to equalise the pressure throughout; moreover, it acts as a water-cushion, especially at the base of the brain.

As the flow of lymph (if we adopt the view that lymph is not in the main a secretion of the lining endothelium of lymphatics) depends upon differences of pressure between the fluid contents of the capillaries and the surrounding cerebrospinal fluid, there is little tendency to a flow from the capillaries into the canalicular system. The canalicular system is particularly well seen in specimens of animals' brains in which an



experimental anaemia has been produced by ligation of the carotids and vertebrals. Figure 61 is a drawing from a section of a monkey's brain in which Dr. Leonard Hill had produced cerebral anaemia by ligation of both carotid arteries and one vertebral. It shews a connexion between the perineuronic space and the perivascular canalicular system. I have examined a large number of animals' brains in which cerebral anaemia was produced in this manner, and I have always observed a similar condition. Although these brains have been hardened in absolute alcohol or corrosive sublimate solution, there were



FIG. 61.—Drawing of a small portion of section, Fig. 60. The large pyramidal cells are seen with their perineuronic spaces filled presumably with a non-coagulable fluid (cerebrospinal). The apical process of one cell is seen in a canalicule which is connected directly with a space around a capillary. It is probable that the cerebrospinal fluid acts as a special lymph of the brain and constitutes the ambient medium of the neuron. These perineuronic and perivascular spaces and their inter-connexions can only be seen distinctly in pathological conditions. The section was stained by Heidenhain's haematoxylin and eosin method. Magnification, 500.

never any signs of coagulated protein, which, if this system contained true lymph, would certainly be shewn.

It may be asked, How is the brain nourished? In starvation, when all other organs waste, the brain does not appreciably do so. We may therefore suppose that the metabolism of the brain is very small, but extremely complex, and the products of activity (probably of a similar nature to those of degeneration), for instance, nitrogenous catabolites, choline, lipid substances, and fatty and lactic acids, are formed and are continually being neutralised and removed by this slightly alkaline fluid. Cavazzani states that the alkalinity of the cerebrospinal fluid is just a little more than half that of blood, and he believes that this depends on the acid reaction of the products of nervous activity. He has proved the existence of a ferment which has an oxidising action on glucose. The cerebrospinal fluid is a secretion possessing properties other than those of



lymph. He has studied this by means of the lymph excitants, injections of which have no effect on the secretion of cerebrospinal fluid.

Of one thing we are certain: that oxygen is necessary for functional activity, and it would be interesting to know what are the oxygen and carbonic-acid tensions of cerebrospinal fluid. The large amount of oxygen which must be contained in the capillaries of the brain to enable it to do its work efficiently does not necessarily mean that all this oxygen is used in directly effecting the bio-chemical changes incidental to neuronie activity; it may be that as fast as it escapes from the blood into the cerebrospinal fluid a substance in the neuron absorbs it and stores it away in a latent state to be used as required, so that the oxygen tension in the fluid is always lower than that in the blood. The experiments of Verworn (p. 210) are of interest in this relation. In connexion with the relations of the cerebrospinal fluid and the nutrition of the nervous system certain characteristics of the neurons as distinct from other cells of the body must be borne in mind: (1) Their marvellous complexity; (2) That although histologically similar, yet physiologically studied in functional groups they differ individually more than any other cells of the body; the corollary to this is that functional variations are more likely to arise in the neurons than in any other cells of the body; (3) Lastly, they are all present at birth, with all their potentialities awaiting the stimuli for the development of their functions and faculties; and if the functions and faculties are not inherited they cannot be developed. Moreover, the neurons are incapable of regeneration, or of lasting beyond their appointed time, even though the conditions of nutrition be favourable. Their progressive differentiation of function, and therefore of structure, has in the long procession of the ages of biological evolution destroyed the power of regeneration. If we accept the material neurological basis of mind, it would be impossible to explain memory (the power of storing away out of consciousness experiences derived from the senses, perhaps, for almost a lifetime to be recollected in consciousness by association) without supposing that the histological elements of mind when once developed and matured undergo little or no morphological change—in fact, are perpetual elements in our organisation. But with such a complex organisation as the cerebrospinal axis, it is essential that it should be protected by a self-adjusting mechanism for uniform equalisation of the blood-pressure under the rhythmical variations of circulation and respiration, and from the chemical products of its own activity, by a fluid which can continually circulate most readily, and yet be the medium of gaseous exchange between the blood and tissues. It is probable that the dextrose contained in the cerebrospinal fluid suffices to produce the energy necessary for neuronie activity, the carbon that it contains being oxidised to carbonic acid. The cerebrospinal fluid, therefore, contains the necessary substances for the functional metabolic activities of the nerve-cells.

*Effects of Increased Intracranial Pressure from Interference with Escape of the Fluid from its Source in the Lateral Ventricles.*—I do not propose to

discuss fully the subject of hydrocephalus, but certain interesting cases which have occurred in my practice, or have come under my notice at necropsies, are instructive. They are cases of internal hydrocephalus caused by non-malignant slow-growing tumours of the third ventricle, and one case of chronic basic meningitis caused by caries of the petrous bone. All four cases had well-marked signs of increased intracranial pressure, vomiting, headache, optic neuritis, tremors, fits, and drowsy stupor, with progressive mental enfeeblement, so that the diagnosis of general paresis was made in all cases except one, which was under my care in Charing Cross Hospital. The patient was a married man, aged thirty-two; the first symptom noticed was that while out walking he was attacked with drowsiness and headache followed by a fit; after this he was the subject of frequent attacks of a similar nature from which he recovered. Eventually he died, and at the necropsy a small tumour was discovered loosely attached to the choroid, which from time to time could easily have taken up such a position as to block the iter, and thus lead to distension of the third and lateral ventricles of the brain. Seeing that the symptoms first came on with drowsiness and headache—this condition ushering in a fit—we may conclude that at this time the tumour had attained such a size that if by chance it fell into such a position as to block up the iter to the third ventricle, the fluid secreted by the choroid plexus accumulated in the lateral ventricles, which would of course necessitate the prone position and possible dislodgment of the tumour, thereby the fluid would escape into the subarachnoid space, and the patient sooner or later return to his normal state of consciousness—at least this was so in the earlier stages of the illness. Here we have a condition of cortical anaemia produced, followed by effects like those of an experiment, namely, drowsiness, loss of consciousness, succeeded by epileptiform convulsions, and towards the end a persistent dulness of comprehension, failing memory, and slowness of ideation—the result of changes in the cortical cells. (For a full account of this case see No. 24.) Doubtless the drowsy stupor and lethargy which come and go in syphilitic basic meningitis are largely due to internal hydrocephalus, produced by the obstruction to the outflow of cerebrospinal fluid secreted in the lateral ventricles by the choroid plexus. As soon as the pressure rises to a certain degree the obstruction is overcome, and an escape takes place into the subarachnoid space, whence it can flow from the cranial cavity in the manner previously indicated. These symptoms of internal hydrocephalus, moreover, support the view that the cerebrospinal fluid is, for the most part, secreted by the choroid plexus contained in the lateral ventricles.

*Abnormal Chemical Changes in the Fluid.*—Is the pia-arachnoid an impermeable membrane? that is to say, do substances circulating in the blood pass into the subarachnoid space, and can they be detected in the cerebrospinal fluid? According to Magendie, potassium iodide can be detected in the cerebrospinal fluid after its administration, and he suggests that it is in this way that the iodide acts upon the nervous

structures in disease. Sicard, however, maintains that the pia-arachnoid is impermeable. If, however, certain drugs—for example, morphine, potassium iodide, cocaine—be injected into the subarachnoid space, toxic effects are produced in accordance with the quantity introduced and the seat of introduction. The injection of cocaine and stovaine by lumbar puncture has been resorted to by many surgeons, especially in France, and a complete anaesthesia has been produced so that operations on the urethra, abdomen, and lower extremities have been performed with complete success, the patient never losing consciousness, but suffering no pain. Certain observations have been made shewing that the composition of the cerebrospinal fluid does become altered in disease—for example, in uraemia urea is present in appreciable quantities, in diabetes the sugar is increased, and when the sugar in the blood and urine diminishes by dieting, the sugar diminishes correspondingly in the cerebrospinal fluid; and it is stated that in pneumonia and those conditions in which the chlorides are retained in excess in the blood, they are increased in the cerebrospinal fluid. As a rule, the fluid is not bile-stained in jaundice. We may, however, say that the slight variations of the fluid which are met with in pathological chemical conditions of the blood all favour the view that the fluid is a secretion of the special epithelium covering the choroid plexus which would prevent these substances passing through. Moreover, the fact that the brain is very seldom stained by the bile in jaundice, unlike other tissues of the body, supports the view that I took with regard to the lymph-supply of the brain. Yet, unless we admit the passage from the capillaries of substances circulating in the blood, whether crystallised or colloid, how can we explain the action of poisons on the nervous system? When they do appear, it is probably by osmosis from the blood into the canalicular systems. Prof. Halliburton and I have shewn that choline, a product of myelin degeneration of the nervous system, may be detected chemically and physiologically in the cerebrospinal fluid and the blood in cases in which there is active degeneration of the nervous system. Moreover, I have found in all cases in which active degeneration is proceeding, and especially therefore in general paralysis of the insane, lipid substances (products of degeneration of the phosphatides), cholesterol, excess of globulin, and nucleoprotein.

*Organised Elements in the Cerebrospinal Fluid.*—(a) *Leucocytes*; (b) *Micro-organisms*.—It has already been pointed out that the cerebrospinal fluid is a clear liquid, which, if centrifuged, contains no organised elements. Lumbar puncture has been practised as a means of diagnosis with great success. At first it was thought it would be valuable as a means of treatment, but in this respect I think it has completely failed, and is practically given up.

Widal, Sicard, Ravaut, Abadie, Karwacki, followed by many others have shewn that leucocytosis of the cerebrospinal fluid is one of the earliest signs of an organic disease of the nervous system. The acute diseases are associated with polynuclears, the chronic with lymphocytes.



In diseases of the nervous system, in which also the membranes are affected, the mononuclears are in evidence—as in meningo-myelitis syphilitica, tabes, progressive paralysis, syphilis of the central nervous system, disseminated sclerosis, and herpes zoster. In functional neuroses and psychoses and in neuritis of various forms there is no lymphocytosis.

Now, it has been shewn by Sicard that injections of oil or coloured particles—such as Indian ink—into the subarachnoid cavity cause a leucocytosis; we may therefore reasonably suppose that the leucocytosis may be in response to the escape of the products of degeneration into the cerebrospinal fluid.

Red blood-corpuscles are not found in the cerebrospinal fluid except in cases of haemorrhages; it is isotonic to the red blood-corpuscles, and therefore they would remain unchanged; but Sabrazès and Muratet have called attention to the phagocytic functions of the endothelial cells lining the subarachnoid space. These are large oval or round cells, 17 to 30  $\mu$ , with an oval nucleus, the surrounding protoplasm containing blood-corpuscles, or the crystalline or other products of their disintegration. The existence of these macrophages in centrifuged fluid would lead to the diagnosis of haemorrhage.

Fortunately, it is only under exceptional conditions that the cerebrospinal fluid contains micro-organisms. Although the blood may contain micro-organisms in abundance, yet the cerebrospinal fluid may be, and usually is, quite free. There are, however, certain conditions in which micro-organisms are almost invariably present—for example, cerebrospinal meningitis, and also in tuberculous meningitis. Although in nearly all cases of sleeping sickness the *Trypanosoma gambiense* has been found in the cerebrospinal fluid, neither in syphilitic meningitis nor in general paralysis and tabes has the *Treponema pallidum* been demonstrated in the centrifuged fluid; although Hoffmann has successfully inoculated animals with blood-free cerebrospinal fluid of a patient with secondary syphilis.

It is of interest to know how the infection occurs; it is certain that when once infective organisms have invaded the subarachnoid space, they find a very suitable medium for their rapid development, no matter what be the seat of entrance; just as pigment particles become generalised in a short time throughout the subarachnoid space and its annexes, even finding their way into the lymphatic glands, so also do infective micro-organisms become disseminated, setting up thereby a generalised cerebrospinal meningitis. Whereas the infective micro-organisms, for example *Diplococcus intracellularis*, the pyrogenetic organisms, pneumococcus, streptococcus, staphylococcus, gonococcus, produce polymorphonuclear leucocytosis, the tubercle bacillus, the syphilitic virus, and the trypanosome of sleeping sickness are associated with lymphocytosis (*vide* Vol. II. Part II. p. 221).

The experimental injections of Flatau already related suggest that there are perineural and perivascular lymphatic connexions between the nasopharynx and the subarachnoid space, and very probably this is the mode of infection by the pneumococcus, *Diplococcus intracellularis*, and in



tuberculosis and syphilis, especially when the lymphatic glands in the neck are infected; otherwise we must suppose that the infection occurs by migrating leucocytes containing these micro-organisms, which is contrary to the experimental evidence I have already referred to, and to which I shall now give more particular attention. Netter has shewn that a haemic infection of the rabbit with the pneumococcus may cause pneumococcic meningitis, but these animals are susceptible to the organism, however introduced into the system. The dog is resistant to subcutaneous or intravenous injections of this organism; but if small doses of the same culture be introduced into the lumbar subarachnoid space, or the cerebral subarachnoid space or the brain substance, a generalised fatal meningitis is set up within a few days, and the heart blood swarms with the organisms. Similar results were obtained with anthrax. Sicard records some interesting results with regard to tetanus. If tetanus toxin be injected into the subarachnoid space the results are more rapid than with subcutaneous or intravenous injection. He maintains that the cerebrospinal fluid in tetanic intoxication of the blood-stream does not acquire any tetanising property; and in three human cases of tetanus it only gave negative results. This is an argument against the cerebrospinal fluid being the medium of exchange between the blood and the nervous tissues.

Tubercle differs from the previously described infective organisms in the slow evolution of symptoms and in its lymphocytic reaction. If tuberculous toxin be injected into the subarachnoid space, death is produced in animals in three to thirteen days, and after death the cerebrospinal fluid is found turbid with leucocytes; there is intense cerebrospinal congestion, without any distinct exudation or granulations.

1. *The Microscopical Examination of the Cerebrospinal Fluid.*—The operation of lumbar puncture is a simple one. It is best performed with the patient in a sitting position, the back bent well forward. After thoroughly cleansing the skin, a large hypodermic needle of about  $1\frac{1}{2}$ -millimetre bore is introduced from without inwards about  $\frac{1}{4}$  inch from the middle line between the third and fourth lumbar spines. This level is below the cord. The fluid withdrawn may be used for (1) microscopical and (2) chemical examination.

(1) The fluid is shaken to distribute the cells evenly, and a drop is then placed on a Thoma-Zeiss haemocytometer slide and all the cells counted on the whole 400 squares. This number multiplied by 10 gives the number of cells in one cubic millimetre of the fluid. Several counts should be made and the average taken. The result gives a rough estimate of the number of cells present, but cannot be regarded as being strictly accurate. The fluid is then centrifuged and the supernatant fluid poured off. The residue is removed in a capillary tube, blown on to a slide, and allowed to dry. The residue from a normal cerebrospinal fluid stained with the Leishman or Jenner stain will shew at the most only two or three lymphocytes in the field with a magnification of 400 diameters, whereas in progressive parasymphilitic

and syphilitic meningitic affections the lymphocytes are greatly increased in number. The amount of lymphocytosis is an index of the activity of the disease; it can also be used as an indication of the effect of antisyphilitic treatment. I have observed the lymphocytes diminish considerably, and the signs and symptoms diminish correspondingly in cases of syphilitic spinal meningitis under treatment. Numerous cases have been recorded illustrating this important law. Lymphocytosis in tabes and general paralysis does not diminish with antisyphilitic treatment, and this method is therefore useful in estimating the effect of treatment as a means of diagnosis in a doubtful case.

(2) Bio-chemical Examination of the Cerebrospinal Fluid.—In order that the reader may have a better understanding of the altered bio-chemical and chemical conditions of the cerebrospinal fluid in diseases of the nervous system, a slight digression in reference to the nature of lipoids is necessary. These substances are of supreme importance in connexion with the pathology of the nervous system, and have recently attracted a great deal of attention in connexion with haemolysis. "There seems to be a good deal of truth in the opinion of Bang that the importance of protein as a carrier of life (*Träger des Lebens*) has been over-estimated, whilst that of the lipoids has been neglected." Pflüger and most physiologists have taught that the vital activities depend essentially upon proteins. Bang contested this exclusive view. The name lipid was given by Overton to *fat-like* substances which are contained in the cells of all living things, animal and vegetable. These lipoids may be divided into three groups—(1) N- and P-free; cholesterol, fatty acids, and lipochromes; (2) Nitrogenous but P-free cerebrosides; (3) Phosphatides containing both N and P; of these the most important are the monamino phosphatide *lecithin* and the diamino phosphatide *sphingomyelin*.

These lipoids were, until recently, considered of little importance; in fact, cholesterol was looked upon as a physiological curiosity because its crystals had a chip out of one corner, and little else was said about it except that it was contained in the red blood-corpuscles and formed the principal constituent of gall-stones. Lecithin was known to be a constituent of the red corpuscles, but it was not until Flexner and Noguchi's experiments on cobra venom had been published that the importance of these bodies in the action of toxins aroused attention. They found that cobra venom contains two poisons, a neuro-toxin and a globulin which has the property of dissolving red blood-corpuscles. If, however, they washed the red corpuscles free of serum, the cobra venom no longer had a haemolytic action; but, on adding serum to the washed corpuscles, an addition of the cobra venom produced haemolysis. Clearly something was contained in the serum which interacted with the venom to produce the result. Kyes shewed that the activator is soluble in alcohol and in ether, and he finally identified the substance as lecithin. But cholesterol, another lipid, has the property of counteracting the activating effect of lecithin on cobra venom. This antagonism of cholesterol and lecithin

points to some bio-chemical or bio-physical relationship between the two bodies. Moreover, this relationship as regards osmotic membranes and haemolysis has been experimentally put to the test by Panucci. This observer constructed glass cells covered with a membrane impregnated with lecithin and cholesterol; in these he placed haemoglobin solution and then suspended them in the toxin solution; the haemoglobin behaved differently (as regards diffusion) according to the proportions of these substances in the membrane. (For further information the reader may consult Rosenheim.) If we regard the red blood-corpuscles as consisting of a sponge-like protein stroma holding the haemoglobin in solution, the whole being covered with a membrane consisting of a properly adjusted complex of the lipid substances, cholesterol and lecithin, then we may suppose that haemolysis occurs as a result of a chemical or physical disturbance of the balance between the cholesterol and lecithin. In haemolysis either the membrane is dissolved by the action of a ferment, or else a physical change occurs in it whereby it becomes permeable to the large haemoglobin molecules, whereas in its natural perfect state it only allows such smaller ions, as Ca, Na, and K, to pass through. It is probable that all cells and unicellular organisms possess similar osmotic membranes, and that the lysis of these organisms depends upon physical or chemical changes, in the osmotic membrane which is termed a periplasium. The importance of this question is obvious in regard to cytolysis, bacteriolysis, and protozoolysis, and it will become especially apparent when we come to the study of the Wassermann reaction of the deviation of the complement in the sero-diagnosis of syphilis.

In regard to the origin of lipoids, especially in pathological conditions, we must first refer to an important paper by Munk. He used the polarising microscope to distinguish between fat and lipoids in cells; lipoids shew double refraction when the analysing Nicol's prism is rotated. Ambrose and Held made use of this method for determining the existence of the myelin sheath in the anterior and posterior roots of the embryo. Munk finds that the existence of lipid droplets in the cell is associated with dissolution of the nucleus and destruction of the cell. Rosenheim remarks that the phosphatides may form a link with the cell nucleins which possibly obtain their necessary supply of phosphorus from this source. A lipid substance in great abundance, then, means cell dissolution; the nucleus highly charged with phosphorus and the cell protoplasm break up into a lipid complex as a result of the nucleolysis and plasmolysis. This fact is of importance as it explains the invariable presence of relatively large quantities of lipid substances, for example, the phosphatides and their cleavage products, and cholesterol, in the cerebrospinal fluid in diseases of the nervous system when there is a degeneration occurring either from ischaemic softening, Wallerian degeneration, or primary decay of the neurons, as in general paralysis and tabes. Seeing that the vascular changes will not account for the decay and the wasting in the former disease if it is progressive and excessive, it is conceivable that a process



of lysis of the neurons occurs, brought about by an alteration of the limiting membrane of the ganglion-cells, caused by a bio-chemical change in the lipoids forming it. These substances escape into the cerebrospinal fluid together with the globulin and nucleo-protein constituents of the cells, and thus account for its altered chemical composition and the reactions which it gives. Moreover, this alteration of the fluid being constant may act as a constant irritant, and set up the characteristic microscopical changes, namely, the lymphocytic and plasma-cell infiltration, and granulation of the ependyma of the ventricles from glial and epithelial cell proliferation. But mere breaking down of the nervous structures secondary to ischaemia will not produce these changes, nor will the fluid give the Wassermann reaction. A specific globulin must be present, and it may be that this, activated by the phosphatide lipoids, produces at first hyper-excitability and then destruction of the neurons, followed by a progressive hyperplasia of the neuroglial, endothelial, and epithelial structures. These cells are stimulated to growth by the inability of the neurons to take up the abundant nutriment now at their disposal; all the while the neurons were in a state of bio-tonic equilibrium they as servants had to be content with a feeble metabolic exchange, but as soon as the neurons, either from toxins or other causes, cease to have the power of assimilating, the satellite glia-cells at once become active and proliferate (*vide* Fig. 58).

Although it has now been ascertained that the syphilitic virus induces in the body metabolic changes whereby larger amounts of lipoids occur in the serum, and also in the cerebrospinal fluid in general paralysis and tabes, yet these same lipoids are found in the normal tissues and fluids—the specific character is manifested by quantity rather than quality. The substances which in haemolysis play the part of *antigens* are lecithins, combined with other substances, especially soaps (Rondoni and Sachs), and those which play the part of *antibodies* are possibly complexes of lipoids and globulins. Yet, although in describing the Wassermann and other methods, and the evolution of the knowledge concerning the same, the terms antigen and antibody will be used, it is better to state at once that they do not conform to the antigen and antibody of bacteriolysins, and that the deviation of the complement (or fixation of the complement) may possibly depend upon the presence of those two kinds of lipoids which, as previously seen, play such an important part in the action of cobra venom.

*The Serum Diagnosis of Syphilis by the Wassermann Method.*—To explain the principles of this method it is necessary to make a few introductory remarks regarding its origin. Bordet, in 1901, discovered the phenomenon known as the adsorption or deviation of the complement. At about the same time Gengou discovered a similar phenomenon when working with preeipitins. Wassermann, Neisser and Bruek, Levaditi, Citron, Plaut, Stertz, and others, have applied this method of the adsorption of the complement of Bordet and Gengou to the diagnosis of syphilis by the existence of syphilitic antibodies and antigens in the blood-serum and



cerebrospinal fluid of persons suffering with primary, secondary, and tertiary syphilis, as well as in post-syphilitic, parasymphilitic (or late syphilitic) affections, namely, tabes and general paralysis. The epoch-making experiment of Pfeiffer on bacteriolysins may be said to have afforded the foundation of our knowledge of the principles governing immunity. Bordet, by his observations, came to the conclusion that bacteriolysis by the serum of an immunised animal was due to the presence of two substances, the one destroyed by heat (thermolabile) present in normal serum, the other (thermostabile) a substance which resisted heat ( $56^{\circ}$  C.) and was only present in the body-fluids and blood of an immunised animal. The former is called the cytase or complement, the latter the immune body or antibody (amboceptor, Ehrlich).

Bordet and others, by experiment, found that if the corpuscles of one animal were injected into another of a different species, these corpuscles disappeared with the production in the serum of a specific haemolysin analogous to the bacteriolysins; the haemolytic properties of the serum being due to a specific antibody (immune body) linking up the cytase or complement to the corpuscles. This important discovery led to the possibility of the study of the theory *in vitro* and its practical application to the diagnosis of disease. The same principles determine the production of haemolysins as bacteriolysins, and the solution of experimentally sensitised corpuscles can be used as a precise index of the presence or absence of one of the two unknowns, namely: (1) the antigen; (2) the antibody or immune body. The thermolabile substance cytase (Bordet) or complement (Ehrlich) is contained in normal serum. Bordet holds that there is only one complement in normal serum, and, contrary to Ehrlich, that it is not a specific substance for each antigen, but specific for each animal. Bordet has introduced the terms antigen and antibody; the former to signify any substance which, when injected into an animal, will cause the production of an immune serum; the latter to denote the antagonising substance produced, which is the essential for the immunising action of the serum. Now, if either the antibody or the complement be not present, or be removed, the specific bacteriolytic or haemolytic action of the serum or fluid is lost. Again, if the antibody in the presence of the complement is linked up to the antigen, both the antibody and the complement will be inactivated. To find out if a given serum or fluid—for example, cerebrospinal fluid—contains either the antigen or the antibody is by the experimental inductive method known as the *deviation of the complement*. How is this effected?

We require first to immunise an animal against the blood of some other animal; for this purpose the blood-corpuscles of a sheep are injected into the circulation of a rabbit. The blood-serum of the rabbit is thus made haemolytic to the corpuscles of the sheep by virtue of an immune body plus the normal complement or cytase. The latter can be removed by heating to  $56^{\circ}$  C. for 30 minutes without destroying the former. We have thus the immune body, which by itself will not

dissolve the washed corpuscles of the sheep. If, however, we add the normal serum of a guinea-pig, the amboceptor or immune body links up the complement or cytase and the corpuscles are dissolved.

The second part of the experiment is the deviation of the complement or its neutralisation, so that haemolysis no longer takes place when the serum of the guinea-pig is added to the immune body and the washed corpuscles of a sheep. This is effected by the presence of both antigen and antibody in the fluid to be examined. The serum, or cerebrospinal fluid to be examined, is mixed in varying dilutions with a watery (or alcoholic) solution of the liver of a syphilitic fetus, which will contain the antigen (lipoid). A small amount of the serum of a guinea-pig is then added and the total volume made up to 2 c.c. with saline solution. The series of tubes containing these mixed solutions are placed in an incubator at 37° C. for one hour, and then the sensitised blood-corpuscles are added. (Sensitised corpuscles are washed corpuscles of a sheep in immune rabbit's serum which has been heated.) The mixtures are again placed in the incubator for two hours at 37° C., then taken out and put on ice overnight. The next morning the amount of haemolysis in each tube is estimated. If, on the one hand, antigen (contained in the extract of the syphilitic liver) and antibody (in the serum or cerebrospinal fluid) have been present they have united with the complement before the addition of the sensitised corpuscles, and no solution of corpuscles will have taken place because the complement has been fixed; if, on the other hand, the immune body (antibody) was not present then the complement (cytase) has remained free to act upon the sensitised corpuscles and lead to their solution. A control experiment, using a normal serum or cerebrospinal fluid, namely, one which contains no antibody, must be used at the same time. In order to make the antigen test, the blood-serum or cerebrospinal fluid is used in place of the liver extract, and tested in varying proportions against a serum or cerebrospinal fluid which has previously been proved to contain the antibody in a known amount. Instead of an extract of a syphilitic liver, which is often difficult to obtain, the extract of guinea-pig's heart or rabbit's heart may be used.

In the hands of nearly all trustworthy and experienced investigators this method introduced by Wassermann has yielded most valuable results as a means of diagnosis. It is stated that it is even more reliable than the agglutination reaction for enteric fever. Plant obtained a positive reaction in 80 to 90 per cent of undoubted cases of syphilis by this method. He found the reaction specific; it is not definitely present in a non-syphilitic individual; it enables a diagnosis of the constitutional disease to be made, but not of the organ affected. He did not obtain the reaction with the cerebrospinal fluid in 25 cases of syphilis in which the nervous system was not affected, and in which the serum as a rule gave a positive reaction. This was not to be expected from what has already been said as regards the cerebrospinal fluid and its secretion. It shews that the reaction depends upon the production of some substances

by the tissues of the nervous system themselves. The nature and origin of that substance will be discussed a little later, but reference will now be made to the remarkable unanimity of opinion of all those who have made experiments upon this subject as to the almost certainty with which the cerebrospinal fluid of general paralytics and, to a less degree, of tabetics gives this Wassermann reaction. According to Plaut the reaction may be negative with the cerebrospinal fluid in cases of syphilis of the nervous system, but he obtained a positive result in 94 out of 95 cases of general paralysis with the cerebrospinal fluid, and in every one of the cases the serum gave a positive reaction. In cases of cerebral syphilis the serum was usually positive and the cerebrospinal fluid usually negative; in 70 to 80 per cent of the cases of tabes the cerebrospinal fluid gave a positive reaction. Citron, G. Meier, W. Fischer and G. Meier, Michaelis, Weygandt, Fleischmann, W. J. Butler, and others have obtained similar positive results by this method. At my suggestion my assistant, Dr. Candler, in conjunction with Dr. Henderson Smith, has applied this reaction to a number of my cases in the hospital and asylums with the following results. They examined the cerebrospinal fluid of 100 cases, of which 94 were asylum cases and 6 were in general hospitals; 46 cases of general paralysis were examined, of which 41, or 89.1 per cent, gave a positive reaction by the Wassermann test. The reaction was not obtained in any of the control cases. I have since had a number of tabetic cases tested, and 60 per cent gave a positive result.

For the purpose of diagnosis, therefore, especially of general paralysis, it is a very important addition to clinical methods. Since its application, however, many doubts have been cast upon the interpretation of the facts and the presence of the reactions, especially as to the existence of any specific relation between syphilitic antibodies.

Levaditi and Yamanouchi made a study of the diagnosis of syphilis and general paralysis by the Wassermann method. The results of their researches are very favourable from the clinical diagnostic point of view. Levaditi and Marie found that normal liver can be substituted for the syphilitic liver in the preparation of the antigen, and that the cerebrospinal fluid of general paralytics supposed to be rich in antibodies is devoid of spirillicide properties. These facts shew that the sero-reaction in question, although clinically a specific test for syphilis, has nothing to do with syphilitic antigens and antibodies. Moreover, the active substances of liver extract, syphilitic or normal, contrary to the true antigens, are soluble in alcohol; and the serum-reaction can be obtained with bile salts and with lecithin, or with soap (Sachs and Altmann), cholesterol, and vaseline (Fleischmann), although more feebly. The sero-reaction of syphilis and of general paralysis is the same, and is not due to the intervention of antibody or syphilitic antigen in the usual sense of the word, and has no relation with the *Treponema pallidum*. Landsteiner and Porges have also demonstrated that the extract of the liver owes its particular properties for this reaction to the presence of lipoids and bile salts soluble in alcohol at 80° C. These products are



found not only in the liver, but also in different organs of man and animals. Landsteiner, Müller, and Potzl state that in syphilitic serum substances are present which in the general sense are not antisymphilitic bodies, but which bind up with certain constituents of normal and syphilitic tissues. Moreover, they assert that the blood-serum of animals infected with *Trypanosoma equiperdum* and *Trypanosoma gambiense* contain similar substances which they have called *histaffines*. Yet being a characteristic reaction, it is attributable to the presence in the serum and in the cerebrospinal fluid of certain unknown compounds, which, in the presence of bile salts, soaps, and lipoids of the liver, precipitate and determine the fixation of the complement. Levaditi and Yamanouchi consider that these compounds arising in the organism itself may be a cholesterol ester. Thus it will be seen that these authorities give a new interpretation to the phenomena of the Wassermann method, which, however, in no way militates against its value as a practical method of diagnosis. They also assert that between normal serums and lipoids of the body and specific serums and lipoids there are only quantitative and not qualitative differences; the reaction of Wassermann is provoked by histogenic and not by bacterial substances. They find, moreover, that lipoids serving for sero-diagnosis not only exist in the liver, but in other organs, such as the brain and the corpuscles of the blood. They are probably complexes; into the composition of which lecithin largely enters.

Levaditi, Ravaut, and Yamanouchi have proved that when syphilis leaves the central nervous system intact, although the serum gives a positive reaction, the cerebrospinal fluid does not; this is what would be expected. It is, however, different when the central nervous system is affected even in a slight degree. The cerebrospinal fluid can then acquire properties which enable it to yield the Wassermann reaction. In fact, in the four cases out of the many examined presenting nervous symptoms, which were neither tabetics nor general paralytics, the fluid has twice given a positive, though quite feeble, reaction. One of the cases was of interest. A married woman with a history of probable syphilis of less than four years' duration was admitted, under my care, at Charing Cross Hospital as a case of tabes. Upon examination I diagnosed cerebrospinal syphilitic meningitis (pseudo-tabes). Lumbar puncture was performed, and the fluid was found to contain 370 lymphocytes per cubic millimetre; she was put on mercurial inunction, and in a fortnight she had greatly improved. The lymphocytes were now only 70 per c.mm.; a fortnight later the lymphocyte count was 20 per c.mm., and she was well enough to be discharged, nearly all the symptoms having disappeared. The Wassermann reaction was negative on the last two occasions on which lumbar puncture was performed; it was not tried in the first instance. The existence of numbers of lymphocytes in the spinal canal does not necessarily entail the appearance of substances which in the presence of lipoids engender the phenomenon of Wassermann. Marie and Levaditi found that there is a



parallelism between the rapidity of progress of general paralysis and the degree of intensity of the Wassermann reaction, and with this conclusion Drs. Henderson Smith and Candler agree; no doubt, therefore, there is a connexion between the breaking down of nervous substances and the amount of this complex lipoid substance with which probably the reaction is associated and upon which it in a measure depends.

Neisser, Bruck, and Stern, who made a large number of experiments on apes and anthropoid apes, as well as observations on human beings, conclude that the antigens are not identical with the living virus, nor of the same substance. They do not consider that mercury and atoxyl destroy the antigen, but that treatment by these drugs injures and destroys the spirochaetes. Moreover, it has been found that antibodies exist normally in small quantities in some of the lower apes; it has so far not been found in the higher apes; it is therefore not a new product in syphilis, but it is enormously increased in quantity in this disease. They consider that the work on the serum diagnosis proves a direct association of syphilis with tabes and general paralysis. Immunity to re-inoculation occurs when the virus has become generalised in the blood and lymph (Neisser). It is probable that the generalisation of the virus engenders simultaneously changes in the properties of the serum, by which changes it becomes capable of giving the Wassermann reaction and of preventing re-inoculation.

There are a number of other reactions which shew that a profound bio-chemical change occurs in the blood in constitutional syphilis. Thus, Klausner found that distilled water added to syphilitic serum causes a precipitation due to the amount of a precipitable globulin which syphilitic serum contains. Fornet and Schereschewsky have shewn that the serum of paralytics and tabetics gives a positive precipitin reaction only with the serum of syphilitic patients, and therefore conclude that this observation proves the syphilitic origin of these two diseases.

*Summary.*—The original method of Wassermann, though the most complicated, is regarded by the majority of investigators as the most specific and trustworthy. Whatever the explanation of the facts, all the evidence goes to prove: (1) That these methods in the hands of competent observers afford a valuable means of diagnosis, and are especially useful when applied to the cerebrospinal fluid for the determination of the existence or not of general paralysis. (2) That similar substances, whether antibodies or not, occur in the serum of syphilitic and parasymphilitic persons in quantities which are not found in the serum of normal persons or in the serum of people with other diseases. (3) That similar substances are found in the cerebrospinal fluid of tabetics and general paralytics, and the amount of those substances which cause a deviation of the complement or a precipitation is in proportion to the activity and duration of the disease; that these substances are of tissue origin or arise from tissue destruction caused in some way by the action, present or past, of the syphilitic virus. (4) It is probable that the syphilitic virus excites an increased unloosening of complex

lipoid substances containing lecithin and cholesterol, etc., from the red corpuscles and cells of the body. (5) That this prevails through life, and in certain cases of syphilitic infection, namely, general paralysis and tabes, the central nervous system, which in ordinary circumstances is protected against the loss of its lipid substances, takes part in the process; that this is manifested by the presence of lipoids and globulins in the cerebrospinal fluid, and that these act as antibodies in the reaction. This lipid complex, as well as globulin, increases in amount as the process of neuron decay proceeds. It is probably owing to the presence of these substances that the granulation of the ventricles, so characteristic a feature of general paralysis, arises as a result of stimulation to proliferative hyperplasia of the ependymal epithelium. Choline may also be present owing to decomposition of lecithin, but this may occur in any active degeneration of myelin and is not pathognomonic of any particular disease.

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THE CHEMISTRY OF DEGENERATION OF NERVOUS TISSUES IN RELATION TO THE CEREBROSPINAL FLUID.—Before discussing the chemistry of degeneration of nervous tissues, it would be well to review briefly the various chemical constituents contained therein, and the variations thereof. In the light of our present knowledge we can only refer to groups of substances which may be arranged under the following headings:—

#### I. Lipoids.—

A. Phosphatides—Fatty compounds containing P and N, such as—

(a) Lecithins—Stearyllecithin,  $C_{44}H_{86}NPO_8.OH$ .  
 Margeryllecithin,  $C_{43}H_{84}NPO_8.OH$ .  
 Palmityllecithin,  $C_{42}H_{82}NPO_8.OH$ .

(b) Kephalins—Kephalin,  $C_{42}H_{79}NPO_{13}$ .  
 Oxykephalin,  $C_{42}H_{79}NPO_{14}$ .  
 Peroxykephalin,  $C_{42}H_{79}NPO_{15}$ .  
 Myelin,  $C_{40}H_{75}NPO_{10}$ .

(c) Sphingomyelin— $C_{52}H_{104}N_2PO_9$ .

B. Cerebrosides—Glucosides free from phosphorus, *e.g.*

Phrenosin,  $C_{41}H_{79}NO_8$ .

Kerasin,  $C_{44}H_{88}NO_8$ .

C. Cholesterol,  $C_{27}H_{45}OH$ .

D. A lipid sulphur compound.

II. Extractives.—Organic water-soluble compounds not colloidal in nature; for example, creatine, taurine, hypoxanthine, etc.

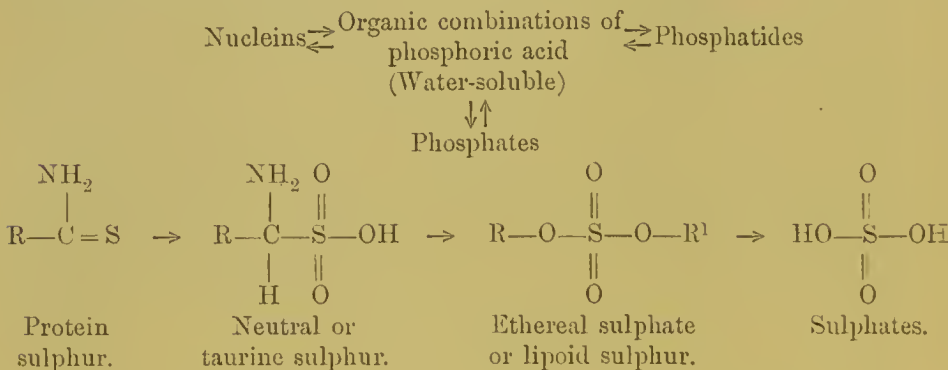
III. Inorganic Constituents.—Na, K,  $NH_4$ , Ca, Mg, Fe, present partly as dissociated ions, and partly in organic combination.

IV. Proteins.—Nucleo-proteins, globulins, neurokeratin.

Analyses of the brain at different ages shew that as adult age is



reached, the lipoids gradually increase, and the moisture, proteins, and extractives decrease. They also indicate that the complex phosphorised lipid substances (phosphatides) and the lipid sulphur compounds are formed by the oxidation of the protein and organic water-soluble compounds of these elements, according to the following scheme:—



It would appear, then, that the normal metabolism of the mature brain depends on the fine adjustment of these oxidation-processes, for analyses of the brain in cases of dementia precox shew a diminution of the lipid and organic water-soluble sulphur compounds, and indicate a general inherent deficiency for oxidation-processes—a conclusion that receives some support from the observations of Pighini on the increase of the water-soluble organic sulphur-compound in the urine in this disease. The necessity of a good oxygen-supply for maintaining the normal metabolism of nervous tissues has been dealt with at length (*vide* p. 200), and these results are of great interest in demonstrating a case in which a disordered metabolism results from the inability of the organism, from toxic or inherent causes, to utilise the oxygen at its disposal. With degeneration, however, there is a general splitting up of the nervous tissues, for analyses of the brain in cases of advanced general paralysis shew that, in spite of the great wasting, the percentage composition is not appreciably altered, except for a decrease in the phosphatides, and a varying increase in the nucleo-protein, accounted for by the glial cell proliferation.

The cerebrospinal fluid bears a direct relationship to the nervous system, and enables us to study the products of the destruction of nervous material. The fluid, which is in excess according to the amount of wasting, shews the most marked changes in the lipid and protein contents.

*Lipoids.*—The most important phosphatides isolated from nervous tissues are (1) lecithins, (2) kephalins, (3) sphingomyelin.

Lecithin is a fat containing in its molecule fatty acids (oleic, stearic, etc.), glycerin, phosphoric acid, and choline. On hydrolytic decomposition these substances are split off. The chemistry of the kephalins and sphingomyelin is more obscure, but it is evident that they undergo similar splitting changes on hydrolysis. Rosenheim and Tebb have recently shewn the presence of sphingomyelin in the mixture “protagon,”



and have found that it yields choline, fatty acids, and a crystalline alcohol on hydrolysis, and differs from the lecithins in not containing any glycerin. In degeneration of the nervous system not only are these phosphatides liberated from the nervous structures, but they also undergo hydrolytic decomposition; the cleavage-products can be found in the blood and cerebrospinal fluid, and the deposition of free fat can be demonstrated by the Marchi method.

The methods for the detection of choline in the cerebrospinal fluid have led to much discussion, for it is evident that choline must be one of a number of similar or even dissimilar cleavage-products from the complex structure of nervous material. Reid Hunt and Taveau have prepared, and investigated the physiological properties of, a number of compounds of choline, some of which, they suggest, may possibly be formed in the body. They found that some of these esters were more active than choline itself, and that acetyl-choline had the greatest physiological activity. They suggested that choline could be detected in the cerebrospinal fluid by the formation of the acetyl and benzoyl compounds; moreover they have noted (*a*) the increased physiological activity of the former, and (*b*) the characteristic crystals benzoyl-choline forms with platinum chloride.

Prof. Halliburton and I first demonstrated the presence of choline in the cerebrospinal fluid by physiological tests, and chemically by the formation of the choline platino-chloride salt. The chemical test was liable to lead to some confusion, for even after repeated extractions of the choline with absolute alcohol it was impossible to eliminate the potassium salts which appear to be in excess in proportion to the degree of degeneration, and which gave similar platinum salts. Rosenheim, therefore, undertook the investigation of the methods for the detection of choline in the cerebrospinal fluid, and concluded that the most trustworthy was in the formation of the characteristic crystals of choline periodide by the addition of a solution of iodine to the concentrated extract of the cerebrospinal fluid. Donath, about the same time, pointed out that the crystals of platino-chloride of choline could be distinguished from the potassium and ammonium salts by the polarisation microscope, in that they are doubly refracting, and therefore appear bright in the dark field, and shew changes in illumination when rotated. Rosenheim confirmed this statement, but found that not all the doubly-refracting crystals gave the characteristic periodide crystals on the addition of iodine solution. I have also found this to be the case, and it is therefore apparent that some of the doubly-refracting crystals may not be choline compounds, but crystals of the platino-chlorides of other organic cleavage-products of degeneration. I have found that by the iodine test all cerebrospinal fluids obtained after death contain choline, and that the test can sometimes be successfully applied to one drop of the fluid; but during life choline can only be detected in cases in which there is marked degeneration, for example, in general paralysis during seizures. It should also be mentioned that in the cerebrospinal fluid of cases of

progressive degeneration of the nervous system, I have been able to isolate an alcohol which bears some resemblance to the alcohol contained in the sphingomyelin molecule; this appears to be present in quantity proportional to the extent of degeneration.

*Cholesterol* is not present in the normal cerebrospinal fluid, but I have been able to detect it in all cases of general paralysis and dementia examined during life. It is also present in all cerebrospinal fluids obtained after death. As far as I could judge from comparative qualitative tests, during life it is present in proportion to the degree of dementia. Pighini has also noted the presence of cholesterol in the cerebrospinal fluid in general paralysis and in other cases with progressive dementia.

The method I have adopted for detecting its presence consists in evaporating 10 c.c. of the fluid to dryness, extracting with hot alcohol, evaporating the filtered extract to dryness, again extracting with alcohol, and again evaporating to dryness, and finally extracting with chloroform, reducing the volume of the filtered chloroform extract to about 2 c.c., and then applying Liebermann's test. This method of extraction I have found to be preferable to the more elaborate and tedious process described by Pighini. Here it is of interest to note the incidence of hard masses containing cholesterol (cholesteatomas) in various parts of the brain and spinal cord in certain senile and advanced degenerative conditions.

*Proteins.*—The most important proteins found in nervous tissues are globulins coagulating at  $47^{\circ}$ - $50^{\circ}$  C. and  $70^{\circ}$  C., nucleo-protein, and neurokeratin, —an albuminoid insoluble in sodium hydrate and not digested by ferments. The amount of protein in normal cerebrospinal fluid is especially low; serum-globulin may be present in slight amount, but albumin is absent. In cases of progressive degeneration, in spite of the large excess of fluid, the amount of protein is found to be greatly increased. This excess consists of globulins, nucleo-proteins, and a small amount of albumin, the greater part being coagulable by heat between  $73^{\circ}$  and  $80^{\circ}$  C. The excess of globulin is the most marked, and Noguchi describes the following method for its detection in a small quantity of blood-free cerebrospinal fluid. Boil for a few seconds two parts of the cerebrospinal fluid with five parts of a 10 per cent butyric acid solution (in 0.9 per cent sodium chloride); add one part of normal sodium hydrate solution (4 per cent), and boil again briefly. Noguchi states that the fluid of parasyphilitic cases gives a granular or flocculent precipitate on allowing the tube to stand for a short time, and that cases of alcoholic psychosis, dementia precox, imbecility, epilepsy, and many other non-specific diseases do not give any precipitate, but that cases of tuberculous meningitis, pneumococcic meningitis, and epidemic cerebrospinal meningitis gave an enormous amount of precipitate. I have applied this test to a considerable number of fluids, and have obtained a positive reaction in many non-specific cases—in fact in all cases of dementia, whether specific or non-specific—and have found that the amount of precipitate is proportional to the degree of degeneration of nervous tissue, being most marked in the progressive degeneration of general paralysis

of the insane. Another test for the globulin present consists in allowing the fluid to flow gently on to the surface of a saturated solution of ammonium sulphate, when a characteristic white ring appears which intensifies on standing. A rough indication of the excess of protein can also be obtained by precipitating the total protein content of the cerebrospinal fluid with three times its volume of absolute alcohol after rendering it faintly acid with acetic acid.

The following is an outline of a rough chemical examination of the cerebrospinal fluid (about 10 c.c.) that may be made in order to approximate the degree of nervous degeneration, by (a) the amount and pressure of the fluid, ascertained while lumbar puncture is being performed; (b) the excess of protein constituents; and (c) the presence of choline and cholesterol. 10 cubic centimetres of the centrifuged fluid, after examination for cells has been made, are taken and rendered faintly acid with acetic acid. 30 c.c. absolute alcohol are added and the whole gently heated on a water-bath for fifteen minutes. After standing overnight it is again warmed and filtered. The amount of protein can be approximated at sight, or weighed on a tared filter-paper or Gooch crucible, the amount of ash being subtracted from the total weight of protein. The filtrate is rapidly evaporated to dryness at a low temperature, the residue is moistened, and a smear transferred on the end of a glass rod to a slide, and one drop of a saturated solution of iodine in 10 per cent potassium iodide solution is added. The mixture is now watched under the microscope, *when, if choline is present, brownish-black rectangular plates of choline periodide will be formed.* The moisture is removed from the residue by evaporation, and another extraction with hot absolute alcohol is made. The filtered extract is evaporated *to dryness* and extracted with hot chloroform. The volume of chloroform is reduced to about 2 c.c., and the presence of cholesterol detected by Liebermann's test.<sup>1</sup>

The test for sugar can be performed on one or more cubic centimetres of the original fluid, and Noguchi's and other confirmatory tests may be made on any remaining fluid.

Many observations have been made based upon the examination of fluids obtained after death; I have found, however, that within a very short time after death, the composition of the fluid so alters that the results obtained are practically useless.

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<sup>1</sup> Add to the chloroform solution a few drops of acetic anhydride, then add concentrated sulphuric acid drop by drop. After a time a rose coloration of the acid, and a violet coloration of the chloroform turning to blue, then green, indicate the presence of cholesterol.



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## TREMOR, "TENDON-PHENOMENON," AND SPASM

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### I. PHYSIOLOGICAL SECTION

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THE physiological basis of "spasm," of "tremor," and of the so-called "tendon reflexes" is a compound reaction from two integrated tissues of the body—the nervous and the muscular. Discrimination between these two factors of composition must be attempted even in the briefest sketch of the subject. The nervous factor will be considered first.

**Nerve.**—*The Neuron as a Transmitter.*—The discharging and conducting elements of the nervous system are its neurons (ganglion-cells), and only they. Each neuron is an eminently excitable cell. The functional waves of change, which it is the office of the nervous system to elaborate and tribute, move along nothing else than a concatenation of neurons. As would be expected in links of a chain, the length of each neuron lies parallel with the direction of transmission of force. At its one end each neuron is an eminently receptive cell, and easy of access by vibrations impinging on its environment: each neuron is throughout from end to end an eminently conductive cell; that is, it readily propagates a change once started in it. Since one end is receptive and the rest of the cell conductive, the waves of change always travel through the neuron from the receptive end. By powerful artificial means a "change" can be initiated in parts of the neuron remote from the specially receptive end; the "change" is then found to be propagated in all directions along the neuron; but in natural circumstances the "change" is always excited at the receptive end only; hence the sense of propagation is never reversed. The "changes" or "impulses," therefore, circulate in one direction only along the nervous system. This is what has been called by James the "law of forward direction." If the outgoing end of the neuron



is turned toward extrinsic—that is, not nervous—tissues, the neuron is *efferent*; if its outgoing end is turned away from extrinsic tissues, the neuron is *afferent*.

*Nervous Impulses.*—Of the "change" or "nervous impulse" inducible in and propagated by the neuron it can be said that it is probably molecular (not chemical), and in quantity almost immeasurably small. Its duration at any one point of the neuron is brief (for example,  $\frac{1}{1000}$  sec.). It travels wave-like along the neuron at a speed of some 30 metres a second, and extends about 10 millimetres on either side of its crest. Some of the neurons in man are 4 to 5 feet long; the duration of the change in them may therefore occupy a large fraction of a second. In the pieces of neurons usually employed for physico-physiological study the wave of disturbance ("nervous impulse") is propagated without alteration in height, length, or speed. But in being propagated along a chain of neurons the "impulse" is profoundly and variously modified. At what points in the chain modification takes place is not with certainty known. It may occur in each neuron at that part whence the stem and other branches of the cell diverge, in fact, at that part which contains the nucleus and is often called "cell body" or perikaryon in contradistinction to "cell branch." An alleged slackening of speed of nerve-impulses through the vagus ganglion is the main datum for this view, which is on the other hand discouraged by the histological fact of unaltered continuity of the primitive fibrils of the neuraxon across the "cell body."

*The Linkage of Neurons.*—A feature of the concatenation of neurons more probably explicative of modification and delay of nerve-impulses is the *synapse*. The successive neurons of the chain do not actually unite, but, although closely juxtaposed, are links retaining separate entity. They are anatomically discontinuous, physiologically continuous. In view of recent histological evidence the doctrine of their conjunction by anastomosis of terminal filaments has been rejected; in its stead points of approximation across varying distances occupied by inter-cellular substance are held to constitute the linkage, such places of linkage of neurons being called "synapses." The reaction of a neuron to excitation is in nature explosive; the relation between stimulus applied to the neuron and change induced in it, is as between a releasing force and a released one. The wave of disturbance evoked in the initial neuron of a chain when transmitted to its outgoing end becomes releasing force for an explosion in neurons next succeeding. The amount of action will depend partly upon the ease with which the disturbance in neuron A can act across the interval between neuron A and neuron B. In other words, the nature of the synapse, and conditions obtaining at it, must to some extent control the conduction along a chain of neurons. Relatively slight exhibition of contractility by the stem or branches of the neuron will greatly affect the width of intercellular gap at the synapse. Slight retraction of this or that cell branch may afford to the neuron isolation from this or that of its neighbours; on the other hand, protrusion may procure greater facility

of communication. The inhibitions of hypnosis may be referable to withdrawal of circumcellular arborisations. Observations by the microscope lend some support to such conjectures.

In the intercellular gap at the synapse between neuron and neuron, not merely the width, but the nature of the ground substance filling it must be apt for the propagation of molecular change across it. In some tissues it is their ground substance which endows them with their functional importance: in the nervous system the properties of that which is the medium of the synapse cannot be negligible. That the direction of nerve-impulses is not reversible along the neural chains may be a function of the nature of a synapse. The synapse is likely enough a bridge open to traffic from neuron A to neuron B, but barred to passage in the opposite sense. It is probable that by these synapses the circuits of the nervous system (Hall's "diastaltic arcs") are as securely valved against regurgitation as is the cardio-vascular itself; hence the Bell-Magendie law, and the "law of forward direction." All synapses appear to lie in the grey matter.

*Variability of Reaction.*—It was stated above that in transit along a chain of neurons nervous impulses may be much modified. Their augmentation or suppression (inhibition), their wide diffusion (for example, in the case of strychnine), or their concentration into a few focal paths, may variously occur. The greater the number of synapses the more variable, the less predicable, the ultimate effect. The reactions which occur along neuron chains of few links only are characterised by "monotony": such are the "simple reflexes." The reactions which employ long chains traversing many synapses are immensely variable; so much so as to simulate the reactions termed "volitional." It is a cardinal feature in the architecture of the nervous system that the longest chains all include cerebral—many of them also cerebellar—neurons and synapses. Hence by removal of the cerebrum the longest concatenations are all broken—although multitudinous shorter ones remain. Accordingly we then find manifold nervous reactions still possible, but all broadly characterised by machine-like uniformity in repetition.

*Latency of Reaction.*—The nervous impulse being a moving, wave-like disturbance, the longer the neural chain the longer, other things being equal, the time which the impulse will take to pass from the initial to the farther end. This time—the reaction period—has for many chains been measured; it is found to increase with greater complexity of the chain far more than with the mere distance of travel in the chain. This increase of "reaction period" seems chiefly proportioned to the number of links—that is, of synapses—in the chain. The "reaction time" for one and the same circuit varies somewhat; but, apart from this, each additional synapse seems to involve marked additional delay in the transmission of the nervous impulse.

*Spread of Reaction.*—The distribution of nervous impulses is obviously dependent on the topographical relations of the neurons and of their stems and branches. Hence in the nervous system minute anatomy

yields much information about paths of nervous conduction. Other things being equal, the nearer together any two neurons lie the more likely the existence of connexions between them. But exceptions to this statement are very numerous. Thus, certain cerebral neurons near the upper end of the Rolandic fissure are more closely connected with certain in the spinal lumbar region than with any in the thoracic or cervical regions. A rule with far fewer exceptions is the following:—each neuron at its "ingoing" end is branched, so that it presents not one but hundreds of points of access; at its "outgoing" end also it is branched, so that it discharges not merely upon one but upon several (perhaps some hundreds of) other neurons; and these rules hold also for the peripheral neurons, connected as they are at one end with non-nervous tissues; thus the motor neuron discharges upon many muscle-fibres. From this rule there results "spread"—the almost universal concomitant of the march of impulses. It is only by synapses that "spread" takes place: the wave of change sweeping within a neuron does not induce waves of change in other neurons even close alongside it (J. Müller's law of isolated conduction), unless by transit across the synapses at its outgoing ends.

*Rhythmic Discharge.*—An important feature of the *discharge* of the neuron is that it tends to be recurrent; that is, the explosion evoked even by a momentary stimulus tends to be repeated a few times. It has been questioned whether one single and sole explosion is ever given by a neuron in reply to excitation applied to it physiologically, that is, via a synapse; but such does seem to have been recorded (Wundt). The prolonged steady action of muscles which characterises "willed" movements is unobtainable by continuous application of any artificial stimulus; but it is imperfectly imitable by certain rapidly intermitting kinds of artificial excitation. Hence, it is argued, the prolonged natural discharges of neurons underlying willed and natural movements are probably of intermittent nature. The hypothesis is supported by abundant evidence of rhythmic activity in muscular and sensifacient cells. The rhythm of the discharge in neurons must vary much, even in the same cell, from time to time. It seems to be slowest when the neuron is fatigued. It ranges probably from 50 per sec. to 5 per sec. We do not know how the discharges from the individual neurons composing a nerve-centre are co-ordinated in time. To consider a concrete case: the spinal motor neurons innervating the flexor brevis pollicis are some 200 in number; they lie scattered through at least three segments of the cord, the last cervical and the two highest thoracic; each of them on entering the muscle throws out a leash of some 30 filaments bearing each a terminal arborisation applied to the motor plate of a column of muscle-cells. It is obvious that the maintenance of willed or other "natural" contraction of the muscle, on the hypothesis of intermittent discharge by neurons, presupposes co-ordination in the time of discharge of the individual neurons. The discharging may take place by volley firing, or by desultory rank firing. On this much-discussed point it can only be said that the general opinion is in favour of volley firing. The failure to obtain



“secondary tetanus” from “natural” movements does not preclude that view.

Observations with the string galvanometer indicate that the action-currents in the flexor longus digitorum muscle of the human forearm during willed contraction follow each other at a rate of about 50 a second, and that in the unfatigued muscle the action-current at each repetition is due to excitation of the muscle by a volley of nerve-impulses, practically simultaneously received by the muscle-fibres throughout the muscle. The number of action-currents per sec. remains the same whether the willed contraction be strong or weak, but the individual currents are stronger for the strong contraction. The rate of repetition of the action-currents is different for different muscles.

*Tonus of Nerve.*—In some circumstances there is a gentle continuous activity of the neuron which is designated its “tonus.” This becomes manifest in the state of the muscle to which the moto-neuron is supplied. In its effect upon the muscle, the tonus appears perfectly continuous; it may, however, be in reality intermittent. Its origin is uncertain. In part it seems to be autochthonous, an inner stimulation of the cell itself by itself, in result of its own metabolism; but it is chiefly referable to mild continual excitation applied to the neuron by other neurons, similarly possessed of tonus, and so placed in the neural chain as to discharge upon it. In tracing the tonus of neurons to its source, one is always led link by link against the current of nerve force—so to say, “up stream”—to the first beginnings of the chains of neurons in the sensifacient fields of the body. From these, especially in the muscles, joints, and otic labyrinth, tonus, constantly initiated, is constantly conducted into the nervous system via the great afferent neurons, the fundamental links of the whole concatenation of the system. The amount of tonus may be varied in several ways. Thus, the tonus of the motor neurons of the spinal cord is much lessened by breaking the neurons of the afferent spinal nerve-roots, the tonus of which latter normally plays upon the former. Chloroform depresses, strychnine augments neural tonus; venosity temporarily exalts and then depresses. It would appear that a certain degree of spinal tonus in the motor neurons is necessary for their appropriate response to the mandates of volition; when the anterior-horn cells have been deprived of spinal tonus, extreme deficiency in certain willed movements immediately results (Mott and Sherrington). And to the tonus of the spinal motor neurons that of cerebral and cerebellar neurons contribute: the cerebral tonus certainly descends mainly from the Rolandic region of the cortex of the heteronymous hemisphere, and is mainly exhibited by flexor muscles; the cerebellar mainly from its homonymous hemisphere, partly in an indirect manner by way of the cerebral hemisphere of the crossed side, partly probably in a less indirect manner through Deiters’ nucleus (Mott, Ferrier and Turner), and is exhibited mainly by extensor muscles. In like manner the tonus of cerebral and cerebellar neurons is the outcome of an interaction of various factors, partly autochthonous, partly of extrinsic, probably especially of spinal origin.



**Muscle.**—We now turn to the muscular element in neuro-muscular reactions. The contractions of muscle-fibres, like the "impulses" of neurons, are explosive liberations of energy; but they involve relatively huge quantities of materials and easily measurable chemical changes. As said above, continuous application of artificial stimuli fails to elicit any continuous contraction of muscle; but by rapidly repeating a momentary stimulus contraction, apparently continuous, can be kept up for a while. This experimental "tetanus" is proved to be really a fusion of simple brief "spasms," each due to a single explosion in the contractile cells. The spasm of contraction started in a muscle-fibre travels wave-like along it, as does the "impulse" along a neuron; but it occupies ten times as great a longitudinal extent, moves ten times more slowly, and consequently is at any one point a hundred times more prolonged. Muscular contractions, although the indices of nerve-discharge most accessible to us, are therefore very coarse indices only. Thus, in physiological tetanus the simple spasms fuse to a prolonged and apparently continuous one, but the exciting cause is, we know, abruptly discontinuous in kind. Again, the intensity of contraction is but an uncertain guide to the intensity of nerve-discharge; the force of an explosion depends less on the size of the spark applied than on the amount of explosive material in store; in the heart-muscle the amount of explosion does not depend at all on the strength in the stimulus applied.

**Tonus of Muscle.**—The "tonus" of muscle, like that of nerve, is of twofold origin. One element in it is "peripheral," intramuscular, autochthonous, exemplary of that tonus resident in all living tissue, vegetal and animal. To this is superadded a tonus of central source contributed from the continual glow of excitement in the spinal motor neuron, whose outgoing end plays upon the muscle-cells, whose ingoing end is played upon by other neurons, spinal, cerebral, and cerebellar. The autochthonous component of muscular tonus is increased by venosity of blood-supply, by mechanical tension applied to the muscle-fibres, by certain drugs, such, for example, as veratria, or digitalis, and so forth. As to the neural component of muscular tonus recent work (43) leaves little room for doubt that reflex tonus is simply the expression of reflex posture. The reflex tonus of the extensor muscles of the limbs, of the retractors of the neck, of the dorsal muscles of the spine, and of the masseters and elevators of the lower jaw is the expression of the postural reflex which maintains the erect attitude. This postural reflex is in other words the reflex posture of "standing." It is traceable to centripetal impulses ascending the afferent nerves of the muscles which themselves exhibit the tonus. Its central mechanism involves besides spinal centres a reflex centre in the brain situate between the anterior corpus quadrigemium and the posterior third of the bulb. The cerebellum and the nucleus of Deiters which lies in that region are in some way closely concerned with this reflex action. The part of the *N. octavus* which comes in from the utricle, saccule, and semicircular canals is also in close touch with it and probably regulates it, but does not appear to be actually essential to it.

This great postural reflex giving tonus to the extensor and other above-mentioned muscles does not give tonus to their antagonistic muscles, for example, the flexor muscles, but rather keeps them slack under a tonic inhibition. It is the muscles (*i.e.* the motor centres of the muscles) receiving tonus in this reflex which are selectively acted on by strychnine and by the toxin of the tetanus bacillus. These agents render this reflex super-active; hence the spasms and rigidities they cause. It is likewise only from this set of muscles that the "tendon-phenomena" are obtained, for example, the knee-jerk, elbow-jerk, masseter-jerk.

Under the conditions of the experiments performed in the laboratory, long-continued spasms, such as constitute "rigidities" at all comparable with those coming under the notice of the clinician, are hardly ever seen. It has, however, been recently discovered that if, in the cat and rabbit, the hemispheres be removed—including the basal ganglia—there ensues in a few minutes a condition of steady extreme extension of the elbow- and knee- and ankle-joints, with retraction of the neck and elevation of the tail. So forcible is this extension that the animal can be placed erect on the four feet; and it requires considerable force to flex the knees and elbows. This extensor spasm may last for several days; it is at first unaccompanied by any perceptible tremor; it can be inhibited by excitation of appropriate sensory nerves; section of the sensory spinal roots causes it immediately to be relaxed in the limb in which the sensory roots are severed. Semi-section of the cord abolishes it below the place of semi-section on the same side. Semi-section of the bulb above the decussation of the pyramidal tracts abolishes it on the same side as the semi-section. It appears therefore to result from an unerossed influence arising somewhere above the lower end of the fourth ventricle and below the cerebral hemispheres. This condition I have called "decerebrate rigidity." It is the most eminently tonic spasm that can be produced by experiment. It appears to be the postural reflex of standing, released from control by higher centres lying in the thalamus and hemisphere.

The bearing upon "spasm," "tremor," and the so-called "tendon reflexes" of the neuro-muscular functions above outlined appears at present disappointingly remote. Whether, for instance, chronic spasm is based on long-continued intermittent neural discharge like that underlying physiological "tetanus," or on excessive tonus of motor neurons, remains obscure. Yet it appears admissible to think that to the physiological qualities of neurons, to their receptivity, conduction, explosive discharge, and tonus—exalted, depressed, or inco-ordinately connected—the abnormal phenomena are referable.

*Tremor in Willed Movements.*—The muscular contractions which execute willed movements are themselves found, when examined minutely, to be often slightly tremulant. The rate of tremor varies from 40 per sec. down to 8 per sec., according to circumstances, the quicker rates being more usual in short sharp movements. The briefest willed contraction endures about  $\frac{1}{3}$  of a sec., its myogram indicating a tetanus of four or five fused simple contractions (Kronecker and Stanley Hall). The briefest

eye-wink takes about .30 sec.; of this time the depressing of the eye occupies .09 sec. (Garten). The briefest willed flexion (for example of a finger) lasts no longer than  $\frac{1}{11}$  sec.; the briefest willed movement is therefore much shorter than the briefest willed contraction; this result is attained by the cutting short of the movement set up by one group of muscles (for example, flexors) by after-coming innervation of the antagonistic group (for example, extensors). The limit set to the frequency of repetition of the same one movement seems to be 11 per sec. The Scherzo of Schumann's No. 8 piano quartette requires rhythmic movement of the hand 8 times per sec. A simple syllable (la) can be repeated about 11 times a sec. The jaw can be depressed as frequently as 7 times per sec.; at the ankle, however, such frequency is impossible.

*Experimental Irritation-Contracture.*—A form of chronic spasm which is of interest in relation to the tremor of willed movements is the so-called "irritation-contraction" observable in the monkey (but not in other laboratory animals) subjected to lesions trespassing on the Rolandic cortex or its subjacent pyramidal path. This chronic contraction supervenes usually on septic mischief complicating a lesion which involves a part only of the Rolandic area. Though a persistent spasm, it is slightly tremulant, with a fibrillar tremor, and is at times a distinct clonus. The muscles affected belong to groups, the cortical centres for which have not been included in the lesion, at least not wholly. It is probably due to chemical irritation of cortical neurons near the wound.

*Experimental Paralytic Contracture.*—A different kind of experimental "contracture," probably rather of the nature of exaggerated "tonus" than allied to muscular "tetanus," follows in the monkey (but not in other laboratory animals) upon total or very large ablations of the Rolandic cortex. It has nothing to do with mere trauma, and usually begins about a month after the healing of the wound. It is hardly, if at all, tremulant. It is a phenomenon whose onset is hastened by want of exercise of the paretic limb. The limb becomes permanently flexed at the elbow or knee, the shoulder or hip being adducted, the ankle flexed. If the animal be encouraged to use the paretic limb freely and in roomy surroundings, or if passive gymnastics are practised, this form of contracture may be indefinitely postponed, and in early stages arrested. The fibres of the affected muscles degenerate after a time; the degeneration affects the stretched extensors more than the contracted flexors; the atrophy is a result of the inactivity. The reason why other laboratory animals do not manifest this contracture is probably because the necessary intensity of paresis cannot be induced in them by brain lesions. A similar "contracture" generally ensues in the hind limbs of the monkey after total severance of the spinal cord in the thoracic region (Sherrington).

The *tendon-phenomena* are clearly and inseparably connected with "tonus."

*The Knee-Jerk.*—It is to the "neural" element in muscle tonus that the tendon-phenomena are intimately associated. The earliest studied of these



phenomena, the knee-jerk, may serve as an example of the class. It is a simple spasm (that is, a contraction due to a single explosion) of part of the quadriceps extensor muscle, usually elicited by a tap or other brief mechanical stimulus applied to the muscle-fibres mediately through tendon. The contraction is a direct reply to a stimulus applied more or less mediately. The reply is obtainable only from muscle-fibres possessed of their "neural" tonus. Of the factors summed in the tonus of the motor neuron, only some appear favourable to the occurrence of the jerk; indeed, the cerebral component restrains the jerk, which is more easily obtained when cerebral neurons have been interrupted, or when cerebral tonus is diverted from the "jerk" neurons to other neurons—for example, on "reinforcement" by claspings the hands (Jendrassik). Also unfavourable to development of the "jerk" is that reflex influence traceable to afferent neurons coming up from the hamstring muscles, the antagonists of the quadriceps (Sherrington). Hence a favourable posture of the limb to elicit the jerk is one insuring relaxation of the hamstring muscles (for example, when the leg hangs crossed over the other). Conversely, an element of the neural tonus very adjuvant to the "jerk" is that developed via the afferent neurons passing between the quadriceps itself and its motor neurons in the lumbar cord: in fact, this latter component of the tonus seems, as regards the jerk, essential; for severance of the sensory spinal root concerned in it permanently abolishes the jerk, even although the tonus derived from other spinal segments and from the cerebrum and cerebellum remain uninterrupted. Transection of the spinal cord above the lumbar enlargement depresses the knee-jerk for a time: in the cat and dog and rabbit for a few minutes only, in the monkey usually for a much longer period, often for several days. Strychnine, it is said, occasionally restores the jerk temporarily, even after section of the sensory nerve-roots; and it is to be remembered that the spasms of strychnine are considered to be reflex. Compression of the abdominal aorta depriving the spinal cord of blood-supply at first exalts, later depresses and abolishes the knee-jerk (Prevost). Chemical anaesthesia rapidly abolishes the knee-jerk. Depriving the peripheral structures themselves of blood—for example, by application of an Esmarch bandage—abolishes the jerk much more slowly; for example, after twenty minutes (Sternberg). Loss of blood causes the jerk to become more brisk (Prns). That increase of the cerebral, cerebellar, and even of distant spinal discharge upon the motor neurons of the "jerk" should antagonise the development of the reaction is probably due to a consequent blocking out of the reflex influence of the local afferent neurons from the motor neurons in question. Under abnormally favourable conditions, the muscular reply, even in response to a single tap, is not a single but a multiple spasm (Adamkiewicz, and others); more so still when the mechanical stimulation is prolonged, for example, by depressing the patella (or in the calf muscles by depressing the heel): a "clonus" then results. The knee-jerk is sometimes spoken of as a "tendon reflex"; no other reflex factor is, however, among the conditions



essential for the jerk than the local spinal tonus mentioned above. The brevity of the time (Westphal, Burkhardt, Waller) necessary for the calling forth of the reaction,—that is, the shortness of interval between the tap and the beginning of the resultant spasm,—excludes the possibility of reflex development. So also with the jaw-jerk. The knee-jerk time, according to Waller's latest measurements, is 0.008 sec.; it must be due therefore to direct excitation. The fact that its myogram shews it to be a simple twitch (Eulenburg, MacWilliam) is therefore what ought to be expected. The time of the crossed knee-jerk is five times as long (Burkhardt) as that of the uncrossed. The crossed knee-jerk may be truly reflex.

A little experience in observations on the knee-jerk imparts a notion of what is to be understood by an average strength of the jerk; just as the average volume and pressure of the pulse are recognised. By this means it is found that wide departures are met with in perfectly healthy individuals, and are recognisable without recourse to such refined methods of measurement as have been employed by Bowditch and Warren, and by Lombard. As a general rule a knee-jerk is "improved" by a preliminary knee-jerk; that is, its latent period is shortened (Brissaud), and the excursion of the movement is amplified (Heller, Meyer). In badly nourished, weakly persons the first tap on the patellar tendon may be ineffectual, and the best jerk responsive to the sixth, seventh, or eighth tap of a repeated series (Schreiber). The same is true of ankle-clonus. Similarly taps on the tendon too light to elicit a jerk at all when applied at intervals of 5 to 10 seconds will ultimately elicit it (Jarisch and Schiff). In sleep the knee-jerk becomes depressed, even to complete abeyance when sleep is deep.

After a certain number of knee-jerks have been elicited the individual jerks become smaller; this seems due to fatigue. Extreme bodily fatigue diminishes the knee-jerk (Lombard), and occasionally abolishes it for a while; the phenomenon returns after rest (Muhr, Jendrassik, Eisenlohr, Sternberg, de Renzi). Fatigue of the extensor muscles of the knee, without general fatigue, has been found by Sternberg and Orchanski to diminish the jerk. Rubbing of the skin of the leg and thigh is an effectual way of increasing the knee-jerk in weakly persons; and it may be thus revealed where at first trial it seemed to be wanting (Schreiber, Weir Mitchell and Lewis). Similarly a cold bath can increase it (Bevor, Dinges, Sternberg); indeed the bath is a more effectual means than any other.

Bowditch and Warren have investigated the time-relations between the moment of application of various accessory stimuli and the incidence of the effect upon the jerk. The accessory stimuli used were cool draughts of air upon the skin or mucous membranes. The maximal amount of increase—of positive reinforcement—of the jerk occurred when the tap on the tendon followed the accessory stimuli at one to three-tenths of a second interval. In most persons the accessory stimulus not merely increased the jerk, but, subsequent to the increase,

diminished it; in other words, the stimulus was favourable to the development of a jerk in response to taps delivered within half a second after its own occurrence, but acted unfavourably to the development of jerks responsive to taps delivered in the second half of the succeeding second. The accessory stimulus ceases to have influence, either positive or negative, after a lapse of 1·7 sec. to 2·5 sec. Westphal noted that when ankle-clonus has disappeared after an epileptiform seizure, a pin-prick of the plantar skin will restore it. Mitchell and Lewis found the knee-jerk increased immediately after a magnesium light had been flashed on the eye. Sternberg recommends the sound of a clapping of the hands as a useful reinforcement just before eliciting the jerk. In 1885 Jendrassik discovered that the execution of a willed movement by the arm renders the knee-jerk for the time being more brisk—"reinforces" it. This is well carried out by asking the patient whose hand holds that of a bystander to grip it forcibly, at the moment at which the knee-jerk is to be elicited. This seems the same thing as that for the obtaining of the jerk it is essential that the patient should let his lower limb "go," in other words, turn his attention from it and let it hang slack. Wundt and Münsterberg argue that a slight degree of contraction of muscles is the physiological substratum of all attention. It is certain that the turning of the attention to the performance of some movement by the arm helps to ensure that looseness and freedom from tension in the thigh muscles which is essential for the provocation of the jerk. The motor cells when preoccupied under cerebral influence appear incapable of the jerk. To remove attention and cerebral influence from the jerk-muscles it is a good plan to tell the patient to fix his gaze on some mark, for example, upon the ceiling; or, in the case of young children, to examine the jerk when the child is feeding; for instance, when taking the breast.

From the above it is seen that at least four modes of reinforcing the knee-jerk are of easy application: (i.) repetition of the tap upon the tendon; (ii.) rubbing of the skin of the limb itself, or still better, the use of a cold bath; (iii.) some stimulus through the special senses, such as by a loud clapping of the hands; (iv.) willed movement of the arm. The importance of these devices for increasing the jerk is well shewn by the fact that Eulenburg concluded from his examination of 338 healthy children prior to the introduction of the reinforcements that the knee-jerk was absent in 16 of them; whereas Pelizaeus and Remak found later, with use of the reinforcements, that the knee-jerk was present in every one of 2403 healthy children examined in succession. The knee-jerk is very brisk in infants and young children; ankle-clonus and a clonic knee-jerk are said to occur in a large proportion of healthy children (Faragó). Möbius states that the knee-jerk is frequently absent in old people of normal health. Sternberg, on the other hand, using the devices for reinforcement, not known at the time of Möbius' research, found that the knee-jerk is probably never really absent in healthy people, even although some of those examined by him were

over ninety years of age. The first effect of general fatigue is to increase the knee-jerk; the ultimate effect, if the fatigue be severe, is to diminish it; sexual excess tends at first to exaggerate the knee-jerk. In winter the knee-jerk is not obtainable in the frog; but in the breeding season it is present. In sleep, as I have said, the jerk is diminished, and in deep sleep quite abolished. I found this so also in puppies in which the spinal cord had been severed in the mid-thoracic region. In these animals I found the jerk less brisk during digestion of a heavy meal than after a day's abstinence.

The influence of the cerebrum on the jerk is seen in the exaggerated knee-jerk obtained in "decerebrate rigidity," and the regularity of time-reaction noted in Rosenheim's experiments. Ziehen has noted the increase of jerk following extirpation of a cortical centre; Adamkiewicz the increase of jerk under gradually increasing cerebral compression. It has been noted that after decapitation in man (executed criminals) the knee-jerk continues obtainable for a minute or more. Regarding any effect of removal of portions of the cerebellum upon the knee-jerk the evidence is not concordant.

*True Deep Reflexes.*—Although the above "jerks" are not reflexes, true reflexes can be elicited by mechanical stimuli applied to tendons, fasciae, periosteum, etc. A smart tap on any accessible tendon generally evokes a responsive spasm in one or more adjacent muscles. Certain bone surfaces are similarly very dependably "reflexogenous." Thus, the inner femoral condyle and the inner malleolus for the adductors of the thigh; the front of the tibia for the quadriceps; the front of the heel or ball of the hallux, also the shin, for the gastrocnemius; the outer edge of the foot for the tibialis posticus; the styloid of the radius for the biceps, less frequently the triceps as well; the wrist end of the ulna for the triceps, less regularly the biceps; the humeral condyles, olecranon, or acromion for the biceps and triceps; the crista scapulae for the deltoid.

The subjoined data may be of service in connexion with the above:—

One "simple discharge" of a frog's gastrocnemius gives an electromotive force of 0.08 volt. The electromotive force of the action-current vagus at each inspiration measures 0.00005 volt (Einthoven).

The branches of the stem-process (neuraxon) of a neuron may offer a cross-section 347,000 times greater than that of the parent stem (malapterurus).

Latent period of direct muscular contraction,  $2\sigma$  (i.e. two one-thousandths of a second).

" " tendon-phenomenon,  $10\sigma$ . Jaw-jerk,  $20\sigma$ .

" " direct muscular contraction recorded by same method as that employed for tendon-phenomenon,  $10\sigma$ .

" " simple reflex contraction,  $30\sigma$ .

Reaction time to touch,  $140\sigma$ .

" " sight,  $180\sigma$ .

The arc employed by the reflex spinal tonus on which the knee-jerk is dependent





is contained (in man) ( $\alpha$ ) in the nerve-trunk of the quadriceps extensor cruris (except rectus femoris), especially in the nerve of the crureus and vastus medius; ( $\beta$ ) in the sensory roots of the 4th and 3rd lumbar nerves (especially of the 4th); ( $\gamma$ ) in the motor roots of the same nerves. The lateral halves of the cord can be split by a median incision without interfering with the arc of the knee-jerk.

#### EXPERIMENTAL DATA CONCERNING "TENDON-PHENOMENA"

##### KNEE-JERK—

Reaction time for knee-jerk (rabbit)	10 $\sigma$	Waller, 1890.
" " " (man)	25 $\sigma$	Eulenburg, 1879.
" " " (man)	30 $\sigma$	Waller, 1881.
" " for conjunctival reflex	50 $\sigma$	Exner, 1874.
" " for crossed knee-jerk	60 $\sigma$	Burckhardt, 1877.

Muscles involved in the jerk (Sherrington, 1892)—

Vastus internus and crureus chiefly, vastus externus slightly, rectus femoris not at all.

Dependent on a reflex arc, of which—

I. The *afferent path* is composed by—

1. Peripheral part—afferent fibres in the nerve of the vastus internus and crureus muscles (Sherrington).
2. Spinal part—afferent fibres in the 5th (chiefly) and 4th lumbar nerves of monkey (the 4th and 3rd lumbar roots of man).

II. The *motor path* is composed by—

1. Peripheral part—motor fibres in the nerve of the vastus internus and crureus muscles (chiefly), and of the vastus externus (slightly).
2. Spinal part—the 5th (chiefly) and 4th (slightly) motor lumbar nerve-root, monkey (4th and 3rd lumbar, man).

III. The *central part*—

Chiefly 5th lumbar and slightly 4th lumbar segment in monkey (that is, in man, 4th and 3rd lumbar segments).

In the monkey (Sherrington), splitting the lumbar cord lengthwise along the median plane does not abolish the knee-jerk. Transection above the 4th lumbar segment usually depresses the jerk for a short time, occasionally suppressing it for a week or more, sometimes not suppressing it at all, even for a few minutes.

Excitation, mechanical or otherwise, of the flexor muscles of the knee—for example, by massage—temporarily depresses and even abolishes the reaction. Similarly excitation of the central end of the nerve supplying the hamstring muscles temporarily depresses or even extinguishes the jerk. Kneeling or stretching the fore tibial muscles has a similar but much less marked effect. Excitation of the skin or of cutaneous nerves appears to have less effect.

The graphic record of a knee-jerk shews that it lasts one-tenth of a second, and



gives on the myographion a curve identical with that of a simple muscle twitch (Eulenburg, 1879).

#### ANKLE-CLONUS—

8-10 movements per sec. Waller, 1882.

#### JAW-JERK—

Reaction time, 20  $\sigma$ . De Watteville, 1885.

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C. S. S.

## II. CLINICAL AND PATHOLOGICAL SECTION

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**TREMOR.**—Tremor is a condition in which the normal, voluntary, continuous, muscular contraction is broken up into a series of minor contractions, which are more or less effectual in attaining the end desired; it may also occur independently of any willed movement, and it may be regularly recurrent, as in paralysis agitans; or irregular, as in alcoholic tremor.

When we call to mind that a muscular contraction is the result of a number of nerve impulses, which follow one another so closely as to fuse almost into one, it is natural to suppose that tremor may be due to conditions which diminish the rate with which these waves succeed each other, and so produce a series of muscular contractions instead of a single one. This supposition is supported by the fact that normal voluntary movements are slightly tremulous, and that fatigue of a neuron makes its discharge less rapid. From this point of view, therefore, tremor may be looked upon as an early stage in the "dissolution" of nerve energy, which, if progressive, would lead to paralysis; and this is seen to be the case in such diseases as alcoholic and other poisonings, and in general paralysis of the insane.

I have recorded several cases of slowly growing tuberculous masses in the internal capsule, in which tremor was the early symptom, and gradually gave way to paralysis as the disease advanced (66).

Remembering the complexity of the anatomy and physiology of the nervous system, we are not surprised to find that this disintegration of nerve impulses travelling towards muscles may result from disease in various situations. While we recognise therefore the great defects in our knowledge of the finer changes which take place in the nerve elements in health and disease, we may take the following as a provisional and rough classification of the conditions which produce tremor:—

1. Deficient or otherwise altered activity of nerve-cells.
2. Inhibition of the action of lower cells by higher.
3. Impediments to conduction,
  - (a) Owing to disease of the conducting nerve-fibres.
  - (b) Owing to disease in the synapses, or in the interstitial tissues about them.

1. **Deficient or otherwise Altered Activity of Nerve-Cells.**—It is probable that tremor does not result from changes in muscles alone, but rather from altered conditions of the nerve-centres and -fibres which call them into action. Even the "fibrillar tremors" of progressive muscular atrophy are due to the slow degenerative changes going on in the anterior cornua of the spinal cord. In the case of voluntary muscles, in which alone we have any experience of tremor, the nerve path is a very long one: originating in the motor centres of the cortex, it passes down in the pyramidal tracts—direct and crossed—to form connexions with the cells in the anterior cornua of the spinal cord; and thence it is continued by the efferent anterior roots to the muscles.

In certain states of general debility—for example, after long illnesses—the enfeebled activity of the whole nervous system is evident, and expresses itself on the motor side in tremulous action of the muscles. A very similar condition is seen in old age, when the lowered vigour of the nervous system is due to the natural diminution in the energy of the metabolic processes which is observable in all the organs of the body.

Between the tremor of healthy old age and that of paralysis agitans there is but a difference of degree. In normal old age the tremor is elicited only when voluntary actions are attempted; but in paralysis agitans the steady flow of nerve energy which passes along the motor tracts, and produces healthy "tone," is also slowed to such a degree that continuous and rapid tremors are produced independently of volitional effort. If a patient suffering from this disease be asked to perform some voluntary act, the additional nerve-energy thus evoked may steady the muscles in action. I have seen a man the movements of whose hands were exceedingly tremulous, who nevertheless could still call forth momentarily steady action sufficient for the purpose of shooting rabbits.

Certain poisons, such as alcohol or mercury, act upon the nerve tissue in such a manner as to give rise to uncertain and tremulous action of muscles. By what means they interfere with the rapid and regular succession of nerve waves is not precisely known.

In general paralysis tremor is usually a very prominent symptom; and depends upon an altered condition of the nerve-cells and -fibres, and of the interstitial tissue which surrounds them.

2. **Inhibition of Action of Nerve-Cells producing Tremor.**—It is well known that certain nerves act in an inhibitory manner upon muscles; moderate irritation of the vagus, for instance, slows the contractions of the heart, and violent stimulation of it may paralyse that organ. But it is also a matter of ordinary observation that disturbances in certain regions of the brain inhibit the action of other regions. Emotions, such as fear and fright, may completely paralyse voluntary muscular actions; and when less intense we see them produce a condition in which, though voluntary movements are performed, they are accompanied by muscular tremor.



It is not improbable that in the numerous cases of chorea which originate in fright, emotional inhibition gives rise to the disorderly muscular action; whilst those cases which are intimately associated with rheumatism are the result of the action of the rheumatic poison upon the central nervous system.

**3. Impediments to Conduction.**—(a) *Disease of nerve-fibres* is not a common cause of tremor; for generally speaking the alteration in the fibres is sufficient to give rise to paralysis. The diseases classed under the head of peripheral neuritis present, as a rule, symptoms of loss of power pure and simple. But tremors are sometimes seen in the earlier stages of alcoholic neuritis, for example, long after the period when they could be attributed to a more general alcoholic intoxication.

(b) *Tremors due to Alteration in the Interstitial Tissues.*—There are certain symptoms of nerve disease which appear to owe their presence to an alteration of the connective tissues which surround the nerve elements themselves; unless, indeed, it be held that all such interstitial diseases are secondary to pathological changes in the more active constituents of the nervous system. The importance now attached by physiologists to the conduction of nerve impulses across the synapses may necessitate a much more careful consideration of pathological alterations occurring in their neighbourhood. Disseminated sclerosis is an example of disease attacking the interstitial tissues and giving rise to tremulous muscular action. It appears as if the presence of this abnormal condition around the nerves produced a difficulty in the transmission of nerve impulses along the tract affected, without absolutely stopping them. Hence what should be one steady continuous muscular act is subdivided into a succession of jerky or tremulous movements in the desired direction.

Now that it has been shewn that the neuraxon of one cell does not communicate directly with another nerve-cell, but breaks up into fine fibrillae about the arborisations of that cell, so that the nerve impulse has to cross the interstitial matter between them, it is quite possible that alterations in and about the synapses may prove to be the causes of some varieties of tremor. In general paralysis of the insane the tremor may be due, to a considerable extent, to the alteration in the substance which links, while it also separates, the nerve constituents of the cortex.

The cerebellum, as a great co-ordinator of muscular actions, might be expected, when diseased, to give rise to tremulous and irregular movements: and so it does; though mainly, if not only, when the central lobe is affected.

We cannot at present be said to possess a scientific knowledge of the pathology of tremor, and the little which I venture to write upon the subject must be taken as in the main speculative.

**Kinds of Tremor.**—From a clinical point of view tremors may be divided into two classes—(A) “Intention-tremors,” and (B) “Passive tremors.”

A. *Intention-tremors*—that is to say, tremors which are produced or, if not produced, are at least exaggerated by voluntary movement.



Disseminated sclerosis affords the most characteristic representative of this class. In this disease no tremor at all exists until the patient attempts some voluntary act, such as raising a glass to his lips. Instead of a steady continuous movement of the arm in the desired direction, a jerky discontinuous movement occurs, the jerks being roughly speaking in the direction of the willed movement. The jerks generally increase in rapidity and diminish in amplitude as the goal is neared. Nystagmus also illustrates well this variety of tremor.

In general paralysis and in Graves' disease the tremors are much finer, but likewise require voluntary action to evoke them. In the former disease they are irregular, and produce a halting and interrupted action of the muscles in action, as is seen in the slow blurred speech of the general paralytic. In Graves' disease the tremor is very fine and vibratory, and does not materially interfere with muscular action.

Mercurial tremor may be constant, but it is increased by voluntary effort.

B. *Passive tremors*—tremors which are independent of voluntary movement.

The most typical example of this class is paralysis agitans. In this disease regular, continuous, fine oscillations are always present, except during sleep. Authors vary considerably in the estimated rate of these various tremors.

Charcot gives	3-6	per sec.	for paralysis agitans.
Peterson "	3.7-5.6	" "	" "
Gowers "	4.8-7	" "	" "
Peterson "	7.9-8.1	" "	for the earlier stages of disseminated sclerosis.
" "	4.6-6.3	" "	for later stages.
Charcot "	8-9 or more	per sec.	for Graves' disease and for alcoholic tremors.

The pathological conditions giving rise to the various tremors which have been mentioned are for the most part tangible anatomical changes in the nervous system, as, for example, in disseminated sclerosis and general paralysis; or they consist in the presence of poisons, such as mercury, lead, or alcohol, which may finally bring about anatomical alterations. But every form of tremulous movement which has been mentioned may occur in the condition known as hysteria: that is to say, disorders of function, which are often transient and destitute as yet of any demonstrated anatomical basis, may closely simulate tremors which are the result of clearly proved pathological changes in nerve structures. It is only by careful consideration of the accompanying circumstances, and of the other symptoms which attend the cases, that a diagnosis between the two classes can be arrived at.

THE TENDON-REFLEXES IN DISEASE.—Authors are now agreed that the normal "tendon-reflex" is not a true reflex, but the direct contraction of a muscle due to tapping its tendon (*vide* p. 299). Inasmuch as a healthy condition of the muscle, as well as of its afferent and efferent nerves and of the spinal centres with which they are connected, is essential to its

production, its clinical importance depends upon the evidence which it affords respecting the state of these structures. Diseases of any one of them causes alteration in the "jerk."

Probably all muscles may contract when their tendons are suddenly "tapped," but only certain selected muscles are examined in this way by the clinician: hence the terms "elbow-jerk," "wrist-jerk," "tendo-Achillis-jerk," "jaw-jerk," and, most important of all, "knee-jerk." So rarely is the latter absent in normal individuals, that its presence in health may be taken as constant (*vide* p. 300).

What is the normal "knee-jerk," or "patellar reflex"—to take this as a representative of this class of phenomena? The reply must be that there is no normal mean in the muscular response to the tap upon the tendon which is found in all healthy persons. There are healthy people in whom it is feeble and difficult to obtain; and there are others, apparently in no better or worse condition of health, in whom it is very brisk. More than this, even in the same individual the "jerk" varies more or less with conditions which can hardly be called departures from health, if indeed they can be estimated at all. This, however, holds true with regard to all the functions of the body; they all vary in health within certain limits: and the clinical difficulty of distinguishing healthy from unhealthy conditions in their early stages depends mainly upon this fact. All one can say is that, as a rule, in normal individuals the "jerk" is a single one, and follows quickly upon the tap on the tendon; but the extent of the "jerk" is variable. Where it appears to be absent at first, it may often be brought out by so-called "reinforcement" (*vide* p. 300). Many sensory stimuli increase the knee-jerk by increasing the tone of the muscles in general; for instance, touching the skin with cold or hot objects, pinching the skin, directing a bright light upon the eye or a loud sound upon the ear: in fact a continuous, though variable, stream of tone-producing energy flows in at all the sensory organs (*vide* p. 300).

It is not, therefore, a matter for wonder that even in healthy people the tendon-reflexes are very variable in degree. In disease they may be altered either in the direction of decrease or increase.

**Diminution and Disappearance of the "Jerk."**—It has already been said that a healthy condition of the nerve and muscle constituents of the reflex are essential to its production. When any one of these constituents is diseased the knee-jerk becomes modified, and nearly always either diminished or absent.

(a) *Disease of Afferent Nerves.*—It has been shewn experimentally that great diminution in the jerk follows section of the afferent spinal nerve: and the lesion in tabes dorsalis is situated in the course of the afferent nerves which enter the posterior spinal root; consequently the knee-jerk is absent in this disease, owing to the loss of muscular tone produced by the lesion. But in ataxic paraplegia, in which to the usual lesion present in tabes is added disease of the lateral columns, the knee-jerk is not absent and may be exaggerated. The probable explanation of this is that, while the disease in the course of the afferent nerve lowers tone,

disease of the pyramidal tract increases it; and this increase more than compensates the diminution due to the lesion in the posterior-root fibres.

In the majority of cases of alcoholic, diphtheritic, and other forms of peripheral neuritis the disease affects both motor and sensory nerves alike; so that in addition to pain and anaesthesia there is also motor weakness. But in some instances there appears to be no motor weakness, and yet the knee-jerk may be absent. This is probably due to affection of the sensory nerves, on the integrity of which tonus depends; a tap then upon the tendon of the atonic muscles fails to produce the jerk. The tendon-reflex is a very sensitive indicator of muscular tone, and it often remains absent for a long time after patients appear to have recovered from sensory and motor paralysis.

Sternberg (*Die Sehnenreflexe und ihre Bedeutung*, 1893) states that the reflex in neuritis may be increased, probably by irritation of the sensory nerves: this condition I have never met with.

(b) *Disease of the Efferent Nerve*.—Peripheral neuritis is due to a very large number of causes, principally poisons of one kind or another—microbic, metallic, alcoholic, gaseous. If they affect the efferent nerve of the reflex arc upon which any of the tendon-reflexes depends, the jerk disappears. The poison of diphtheria and alcohol are well-known examples of this function. In some general diseases, such as diabetes, which lead to great debility, the jerk disappears; sometimes owing to the presence of peripheral neuritis, often, probably, to loss of muscular tone independently of neuritis.

(c) *Disease of the Cells in the Anterior Cornua of the Spinal Cord*.—This is not an uncommon cause of loss of the knee-jerk. In infantile paralysis the jerk is absent. In paraplegia due to myelitis the knee-jerk may be exaggerated or it may be absent. When that portion of the cord is affected from which the third and fourth lumbar nerves issue, it is absent; when the disease is above these lumbar centres, it is exaggerated, owing to diminution of the inhibitory action of the pyramidal tract fibres. In progressive muscular atrophy, which is due to very slow degeneration of the cells in the anterior cornua, the jerks gradually disappear as the muscles get more and more wasted.

(d) *Disease of the Muscle on which the Jerk depends*.—Gross disease of the muscle would, of course, produce loss of the jerk; but this hardly occurs primarily; it is almost always due to affections of the spinal centre which is connected with its motor nerve, or of the nerve itself. Pseudo-hypertrophic paralysis and other myopathies are, however, exceptions to this rule, as they are diseases of the muscles, and not of the nerves which supply them; in them the jerk disappears gradually as the muscles disappear. In conditions of extreme general wasting and feebleness the tendon-reflex may disappear. This is probably due partly to the feeble condition of the muscle, and partly to that of the nerves connected with it.

In traumatic rupture or complete disorganisation of the spinal cord above the lumbar enlargement the knee-jerk disappears, and may remain



permanently absent, or reappear after some time. Why this happens is not clear. If the result were due to shock, the "jerk" should return much sooner than it does. Moreover, when myelitis, or pressure on the cord by tumours, produces apparently complete anaesthesia and complete paraplegia, the knee-jerk does not disappear, but is usually exaggerated. Sternberg asserts from actual observation that in sudden decapitation in man, and in clean division of the cord in animals, the knee-jerks do not disappear: and he argues that their absence in certain traumatic cases is due to the grossness of the lesion, which crushes the cord and irritates the inhibitory pyramidal tracts.

In relation to this question it must be remembered that the condition of muscle which is best adapted to the production of this tendon-reflex, is one intermediate between atony and spasm. Either of the latter conditions will prevent the jerk. In many cases of paraplegia due to lesions above the lumbar centres there is a gradual development of spasm and permanent rigidity of the muscles of the leg; and this rigidity alone renders it impossible to elicit the knee-jerk.

In sudden lesions of the brain producing coma, such, for instance, as haemorrhage, if the coma be profound the tendon-reflexes are absent; if it be not so profound they are present, and even exaggerated on the side opposite to that on which the haemorrhage has occurred. The explanation of this again is not very evident.

**Increase of the Jerks.** — It is very doubtful if increase of the tendon-reflexes ever occurs from a primary affection of the afferent or efferent nerve of the reflex arc, or from alterations in the muscles. And the same may be said in regard to the spinal centre with which these nerves are connected. The only exception which must be made to this statement is that certain poisons, such as strychnine, produce temporary increase of these phenomena. Strychnine is said to do this by its action on the afferent nerves.

Increase of the tendon-reflexes is nevertheless very commonly met with, and in the great majority of cases depends upon disease of the pyramidal tracts. The normal effect of these tracts upon the spinal centres upon which the jerks depend, is to restrain their activity; thus, when they are divided or diseased the tendon-reflexes are increased. As the pyramidal tracts arise in the motor regions of the cortex and traverse the internal capsule, the crura cerebri, the pons, medulla, and spinal cord, it is clear that a great number of pathological conditions affecting the brain and cord will be accompanied by increased activity of the "jerks." In hemiplegia, due to whatever cause, this is the case. In inflammation, tumours, and like diseases of the cervical and dorsal region of the spinal cord, they are likewise increased.

Each pyramidal tract divides; a smaller portion of its fibres descends in the anterior column of its own side, the greater number occupy the lateral column of the opposite side. In unilateral brain lesions, therefore, there is generally an increase of the knee-jerk on both sides, the increase being greater on the side opposite to the lesion. The division



of the pyramidal tract above is liable to great variations, so that most if not all the fibres may cross, or most if not all may be direct; consequently the phenomena of disease vary likewise. If, however, it can be shewn that all the fibres of the pyramidal tract cross, either in the medulla oblongata or later in the cord below, then the bilateral increase of the tendon-reflexes, owing to a unilateral lesion, must depend upon some connexion between the fibres on one side and the anterior cornual cells on both sides.

In the subjects of neurasthenia, whose whole nervous system seems to be in a feeble condition, the tendon-reflexes are, as a rule, increased. This may be due to the cerebral centres and their efferent pyramidal tracts, as the most highly developed parts of the nervous system, suffering out of proportion to the rest; thus their inhibitory influence over the lower spinal centres is lessened, and the tendon-reflexes thereby exaggerated. In some of the cases referred to, however, the tendon-reflexes are diminished; possibly owing to the neurasthenic condition affecting the centres in the cord as well as those in the brain.

There are a certain number of cases in which the tendon-reflexes are diminished or absent, although the reflex arcs are healthy and the disease situated in the central nervous system above them. Such a case I have lately seen, in which violent pain in the head, vomiting, optic neuritis, and mental dulness, lasting for some months, indicated the presence of a cerebral tumour. There was no paralysis, motor or sensory. The knee-jerks could not be elicited. The explanation of such cases, which occur from time to time, and of cases of cerebellar disease, in which the tendon-reflexes may be normal, diminished, absent, or exaggerated, cannot at present be given. Sternberg suggests that slight degrees of irritation of the pyramidal tract fibres may increase their inhibitory influence and prevent the tendon-phenomena; but in the case quoted above there was no evidence of any irritation producing increased tone, which in such circumstances we should have expected. We know that the general muscular tone of the body depends largely on ingoing sensory stimuli of all kinds, which flood the nervous system with energy; these may come from sensory organs, but they also originate from active intellectual and emotional operations. It is quite possible that at present we underrate these influences, and that the stoppage of such stimuli, owing to disease of certain portions of the nervous system, may depress or extinguish the tendon-phenomena—just as division of afferent nerves in the cord has been experimentally shewn to do.

**Clonus.**—As already remarked, when the inhibitory influence of the pyramidal tract has been diminished by disease, increased tone is produced in the spinal centres below the lesion, and the tendon-reflexes are exaggerated. In a later stage, when the lesion in the course of the pyramidal tract has very seriously damaged the fibres, rigidity of the limbs sets in. But there is an intermediate stage in which clonus appears, and usually multiple "jerk"; that is to say, when the patellar tendon is tapped, instead of one knee-jerk several may occur in

succession. In healthy persons placed in such a position that the patellar tendon is slack, no contraction of muscle follows sudden depression of that bone. But when "tone" is increased, sudden muscular contraction is produced. If "tone" be still more increased stretching the patellar tendon, by sudden depression of the bone, results in a series of muscular contractions. The same occurs when by sudden flexure of the foot the tendo Achillis is stretched. This phenomenon is called clonus. Whilst simple exaggeration of the knee-jerk informs us that the tone of the muscle is heightened, clonus means that "tone" has been still further increased; and in most cases it is owing to increasing paralysis of the pyramidal tract fibres. Hence we look for clonus at a later stage of all those affections of the brain and spinal cord, already referred to, which produce increased "jerks." Just as one speaks of the "knee-jerk," "tendo-Achillis jerk," "jaw-jerk," "wrist-jerk," and so forth, so we use the corresponding terms "knee-clonus," "foot-clonus," "jaw-clonus," "wrist-clonus," and the like.

It happens occasionally that ankle-clonus is present and the knee-jerk absent in the same case. This association is due to a lesion which destroys the lumbar centres on which the integrity of the knee-jerk depends, and at the same time interferes with the fibres of the pyramidal tracts which control the lower centres presiding over the nerves connected with the tendo Achillis and its muscle.

**Babinski's Sign.**—In 1898 M. J. Babinski called attention to an alteration in the plantar reflex which occurs in cases of disease of any part of the pyramidal tract. Though not a "tendon-reflex" like the knee-jerk its significance is similar to that of increased knee-jerk and clonus. In order to examine the plantar reflex the patient should be lying on his back in bed, and the most favourable position of the leg is resting on a pillow, semiflexed at the knee and hip and rotated outwards. In the normal individual if the sole of the foot be gently stroked with the finger, penholder, pin, or the like, the four outer toes and finally the great toe slowly flex, the ankle is dorsiflexed, and the foot is inverted. When the reaction is vigorous the sole is hollowed, forming a transitory pes cavus. Other and more distant muscles, such as the tensor fasciae femoris, may also contract, but the reaction described above is the important one on which the attention is to be fixed. The plantar reflex may be absent in gross disease of any part of the reflex arc, and is often absent in functional conditions too, and when the feet are cold and damp.

The interest of Babinski's sign from the point of view of the present article is, that in diseases affecting the pyramidal tract, the plantar response is no longer flexor, but becomes extensor: and this change is an early sign of such disease, earlier than ankle- or knee-clonus, nor does it, so far as is known, occur in functional disease. When the sole of the foot is gently stroked the great toe is extended at the metatarsophalangeal joint, and extension of the outer toes may follow together with dorsiflexion of the ankle and inversion of the foot. The signal of the reaction, however, is the great toe; and the more one limits the

response by gentle treatment of the sole to that toe, the more reliable it is. For one must remember that the natural involuntary withdrawal of the foot from violent or painful irritation of the sole is not only sudden flexion of hip and knee, but also dorsiflexion of the ankle and extension of the toes. The extensor plantar response may in rare instances be absent in cases of disease of the pyramidal tract; but when it is present it is a sure sign of the latter. One exception must, however, be borne in mind. In young children the pyramidal tract is in an undeveloped condition, and until the child walks the plantar response is extensor. In older children, too, it may remain extensor during sleep, though it becomes flexor on waking. With these exceptions the extensor plantar response is a most valuable sign of disease of the pyramidal tract: but we are not infrequently at a loss at the bedside as to whether it is present or no, owing to the ill-defined or variable response which is given by the admixture of voluntary action on the part of the patient with what ought to be a purely reflex act.

SPASM.—By spasm is meant excessive muscular contraction; and, in the case of those muscles which are under the control of the will, excessive contraction is that which occurs in defiance of the will; or which, although beginning as a voluntary act, transgresses the limits which the will would impose upon it.

Where involuntary muscles are concerned the definition of "excessive" is more difficult. When the muscles of the intestine, for instance, make spasmodic efforts to drive along the contents of the bowel through a portion which has been narrowed by disease, so far from the muscular action being excessive, it may be insufficient for the purpose. In such a case, and in others of a similar kind, it can only be said that spasm is muscular contraction which exceeds that which occurs in conditions of health, and in the course of the normal physiological processes.

Muscular spasm is, for the most part, a nerve phenomenon; though it probably occurs sometimes from causes acting directly on the muscular fibres. "Cramp," for instance, may sometimes be due to the circulation in the muscles of poisons originating in deranged digestive processes, or in abnormal metabolic changes in other parts; or perhaps inflammation of the fibrous sheath of the muscle itself may produce it. Still it may be accepted that the nervous system is responsible, as a rule, for the occurrence of spasm in muscles.

Some cases of distortion of limbs appear at first sight to be due to muscular spasm, when in reality they are not so. Take, for example, the claw-hand in progressive muscular atrophy: here atrophy of the interossei muscles occurs, and, the opponents continuing to act normally, hyper-extension of the proximal and flexion of the peripheral phalanges of the fingers occur. But there is in reality no overaction or spasm on the part of the extensors: equilibrium is overthrown by atrophy of their antagonists; hence the distortion.



Another instance of a similar kind is found in the disease called "pachymeningitis cervicalis," in which the distortion varies according to the position of the disease in the cervical region. If that part be diseased from which the median and ulnar nerves emanate, the muscles supplied by the intact musculo-spiral produce that form of distortion in which the wrist is extended; whilst, if the upper half of the cervical region be the seat of the disease, the muscles innervated by the median and ulnar nerves produce quite a different condition, one in which the wrist is flexed.

Looking at the subject from a clinical point of view, the following varieties of spasm may be observed.

**Kinds of Spasm.**—1. *Tonic Spasm or Contraction.*—This is a constant steady contraction of the muscles involved, varying from a condition of slightly increased tone up to one of extreme rigidity. It is well seen in the later stages of hemiplegia due to whatever cause; and in cases of paraplegia in which the pyramidal tracts are partially cut off by disease from the spinal centres below. It also occurs in cases of "primary lateral sclerosis," and in porencephaly, in which large defects occur in the cerebral hemispheres, either as congenital malformations or as the result of early disease. The motor centres in the cortex of the brain and the pyramidal tracts which descend from them through the cord are the agents which give rise to contracture. Slight interference with the healthy condition of these nerve-structures results in the loosening of the reins which inhibit the spinal centres; and increase in "tendon-reflexes" is the first evidence given of the change. A little more disease of these tracts, and "clonus" is seen; and, finally, in grosser disease we get "contracture."

2. *Clonic or intermittent spasm*, the second clinical variety, is that in which the muscular contraction is not continuous, but intermittent. Periods of action are succeeded by periods of inaction. The spasm may recur at regular or at irregular intervals, and with every degree of rapidity. These conditions are illustrated in chorea, spasmodic wry-neck, facial spasm, and in many varieties of hysterical or functional spasm.

The causes underlying many cases of clonic spasm are very obscure. But the well-known pathological conditions which produce hemiplegia are not infrequently followed by clonic spasm in the paralysed muscles; thus conditions of athetosis or post-hemiplegic movements of various kinds result.

3. *Tonic and Clonic Muscular Contractions.*—In a third variety of spasm these conditions are combined. This is well exemplified in many cases of congenital defects, or diseases of portions of the hemispheres occurring in early life, which give rise to a porencephalic condition. In them there is a certain amount of persistent rigidity of muscle, combined with frequently recurring movements. The latter are sometimes extremely violent, and may be quite uncontrollable.

If the subject of spasm be looked at more from the pathological point of view, it must be confessed that our knowledge is very defective, and



that many instances of this condition are at present quite inexplicable. A review, however, of the possible, probable, and well-known conditions giving rise to spasm may be useful.

**Spasm as a Symptom.**—1. *Spasm in Relation with the Pyramidal Tracts.*—The connexion which exists between disease in the course of the pyramidal tracts and spastic conditions of the limbs is very frequently exemplified at the bedside. In a large proportion of cases of softening of the brain, whether due to embolism or thrombosis of arteries, and in cases of cerebral hæmorrhage with hemiplegia or monoplegia, contracture often supervenes in the limbs—if they remain permanently paralysed. This is usually more marked in the arm than in the leg, and, the flexor muscles being more powerful than the extensors, more or less flexion at the joints results. This is accompanied by increased tendon-reflexes, and often by clonus. The removal of cerebral inhibition from the spinal centres increases the action of the cells in the anterior horns on the muscles which they innervate; this is curiously illustrated in certain rare cases, in which after its extinction in tabes dorsalis the knee-jerk has reappeared on the supervention of an attack of hemiplegia. The same effect is observed in cases of ataxic paraplegia in which, in spite of disease of the posterior columns, the knee-jerk is exaggerated; the removal of the inhibitory influence of the pyramidal tract, which is also diseased, more than compensating the diminution of the nerve energy which under healthy conditions reaches the anterior cells through the posterior-root fibres. Congenital defects in the pyramidal tract have the same influence on the centres below; and the spastic condition present in the weakened limbs in such circumstances is strong evidence in favour of the explanation which has been adopted as regards the spasm which follows upon diseases of this tract; namely, that it is due to removal of the inhibitory influence which it normally exerts. Disease of the cortical motor centres in the brain produces the same results.

Occasionally the spasm is bilateral although the lesion of the pyramidal tract is unilateral. This is probably explained by the more equal division of the tract at its decussation in the medulla oblongata, so that there are more "direct" and less "crossed" fibres than usual; or, if all the pyramidal tract fibres decussate either in the medulla oblongata or in the cord below, the tract fibres of each side must be connected with the anterior cornua on both sides. In most of the ordinary cases of hemiplegia, though there is not bilateral spasm, there is bilateral increase of the tendon-reflexes. When the lesion interfering with the pyramidal tract fibres is in the cord, as in cases of transverse myelitis and primary softening in the dorsal region, bilateral spasm of the legs occurs.

When spasm accompanies the presence of tumours of the cerebellum, it is probably not due directly to the cerebellar disease, but to the pressure which the tumour exerts on the pons and medulla below.

Contracture, or fixed spasm, is a comparatively frequent result of cerebral lesions which permanently interrupt the nerve-impulses proceeding from the cortex along the pyramidal tract. But, in addition, mobile

spasms have been observed in great variety, either after hemiplegia or independently of it. Sometimes they attend voluntary movements only, sometimes they are involuntary and continuous; but in all of them the retention of a large amount of voluntary control over the affected limbs is a striking feature. In addition to the mobile spasm there is often a certain degree of fixed spasm, though a marked degree of the latter would be incompatible with the development of the former. The names athetosis, post-hemiplegic chorea, and post-hemiplegic inco-ordination are applied to these conditions. The lesion in such cases has been found in various positions—in the cortex, optic thalami, corpora striata, and so forth.

All the varieties of mobile spasm seem to result from a mixture, in varying proportions, of paralysis, spasm, and irritation; and their development depends upon lesions which interfere with the functions of the motor centres and fibres, but which do not interrupt them completely. In cases in which a tumour presses upon the cortex of the brain, or upon the cord, recurring attacks of spasm often precede the continuous rigid contracture which finally sets in. This is probably due to fluctuating conditions of the circulation within the growth, which alter its size and consequently its pressure from time to time.

2. *Spasm due to Disease of Efferent Spinal Nerves.*—In the description which has been given of contracture the active agency in its production has been attributed to the spinal centres; removal of the inhibitory influence of the pyramidal tract induces overaction in them, and spasm, of the muscles which they innervate, results. But does disease of the spinal centre, or of its afferent or efferent nerve, produce spasm? Disease of the motor nerves is far from an unusual occurrence; musculo-spiral paralysis, for instance, is often seen in quite early stages of spinal disease, but muscular spasm is not one of the symptoms. In chronic poisoning by lead and alcohol various nerve symptoms are met with, including paralysis, and even muscular rigidity; but the latter is due to the contraction of the unopposed healthy muscles, and is not produced directly by the diseased nerves. In inflammation of the sciatic nerve twitchings and sudden cramp may be experienced; but they are very transient phenomena. The implication of motor or mixed nerves in a growth gives rise to similar symptoms, in addition to great pain; but well-marked spasm scarcely ever occurs. Clonic spasm is not infrequent in the late stages of facial paralysis, when there is shortening of the muscle from atrophy; the spasm is then due to irritation of the nerve- and muscle-fibres which have survived the process of destruction. The attacks of spasm in spinal meningitis are probably reflex in origin, and not due to direct irritation of motor nerves. The pathology of tetany is doubtful, but there is no good reason for supposing that it has any connexion with irritation of motor nerves (*vide* Art. "Tetany" in Vol. VIII.).

It would appear, therefore, that whilst occasional spasm may occur in peripheral nerve disease, from direct irritation of motor filaments, and

may even now and then be permanent, it is quite exceptional to find it amongst the marked phenomena in such cases.

3. *Spasm in Relation to Disease of the Afferent Nerve and its Centre.*—How far spasm is produced in a reflex way is an exceedingly difficult question. Cases of general convulsions, as well as of local spasm, are frequently explained in this way, and yet the explanations are so incapable of proof that the arguments adduced in favour of such an origin often carry very little conviction. Many such cases occur in which some sensory nerve is the seat of severe pain; or in which a diseased part is painful to move. A good example of the former class is spasm of the muscles of the face accompanying facial neuralgia; of the latter, rigidity of muscles surrounding a painful joint. But the most ordinary method of expressing pain is by overaction of the facial muscles, whilst the ordinary way of preventing pain in joint disease is by keeping the joint still, and opposing attempts at movement by contraction of muscles which prevent it; and it is often very difficult to decide how far the muscular action is voluntary, how far involuntary and reflex.

No one who observes the great variety in the degree of muscular contraction produced by similar stimuli applied to different individuals, can be surprised at finding evidence that persistent spasm may sometimes occur as the product of a reflex act; or that a stimulus which produces no motor result in one person gives rise to definite muscular contractions in another not equally healthy. Thus, in hemiplegia accompanied by descending sclerosis in the lateral columns the deep reflexes are much more brisk than they were before the hemiplegia occurred; and even contractures previously existing may be suddenly increased by comparatively slight injuries. If this increased reflex excitability be due to the hyper-physiological activity of spinal centres which have been freed from cerebral control, similar disorders of nerve-centres rather than of nerve-fibres are probably the most fruitful causes of reflex spasm. Hence it is scarcely too much to say that the injury or disease which supplies the stimulus to the sensory nerve in such cases, though apparently the principal agent in the production of spasm, is really so only from a limited point of view. Were the nerve-centre in a healthy and stable condition, muscular spasm would not occur. Thus in tetanus it is the hyperactive condition of the nerve-centres produced by the specific toxin that gives rise to the muscular spasm.

In speaking, therefore, of reflex spasm resulting from irritation of afferent nerves the nerve-centre must be considered at the same time; for it is questionable how far stimuli applied to afferent nerves could produce muscular spasm if the centres were healthy.

Reflex spasm no doubt occurs, but how frequently it does so, and how far the afferent or efferent nerves, or the nerve-centres, take the leading part in its production, are points which it is difficult to decide. A good instance of reflex spasm was recorded by the late Mr. Chutton. A boy, aged fourteen, had been bitten in the face by a dog eighteen months previously. The spot had been painless until a month before his appear-



ance at the Hospital ; but since that time he had suffered from constant shooting pains in the neck, which always started from the scar. At the same time that the pain was felt the angle of the mouth was drawn outwards, and the skin of the neck was wrinkled by the platysma. The whole side of the neck and face blushed, and then became bathed in perspiration. This succession of symptoms recurred every time the scar was pinched. Butyl-chloral-hydrate in five-grain doses twice a day cured the affection. Weir Mitchell gives instances of reflex spasm ; and similar phenomena are often referred to intestinal, uterine, or other irritation, but not always with sufficient reason.

Children are specially prone to convulsions and spasm ; and it is interesting to remember that in them the pyramidal tracts, the great controllers of reflex muscular contraction, are for a long time incompletely developed. In the brain afferent and efferent nerves and nerve-centres are so closely packed together that it is quite impossible in many cases of spasm of cerebral origin to say which of these takes the leading part in the disturbance.

4. *Spasmodic Muscular Contractions which appear to have the same Explanations as Tendon-Reflexes.*—Muscles contract when they are put on the stretch by their opponents ; and the interaction of the two sets of muscles has the effect of controlling and steadying movements which might otherwise be jerky and uncertain. But a tendon may be overstretched and spasm may result. A medical man took a vehicle in order to drive to a house where he was going to stay for a while. The driver put him down  $2\frac{1}{2}$  miles from his destination and drove off. The doctor had a heavy bag and had to carry it himself. For four days after this he suffered from constant contraction of the triceps muscle of his right arm whenever he flexed the latter. Such a case represents a very small departure from the normal, but it suggests an explanation of more troublesome affections ; such, for instance, as the following :—A girl, aged nineteen, had her wrist sprained and bent backwards five years before she was seen by me. She had been obliged to carry her arm in a sling for some weeks. Ever since then she had suffered without intermission from “twitching in the arm and palm of the hand.” The general power of the arm was found on examination to be unimpaired ; but there were spasmodic contractions of the palmaris longus, which occurred with perfect regularity ninety times in the minute. In such instances it is probable that the spinal centres are in an unstable condition, as such continued rhythmic spasm after a sprain is quite exceptional. Every one is familiar with the ankle-clonus which is sometimes set up in healthy people when sitting with the toes on the ground and the heels a little raised. If the clonus be once started it may be difficult to stop it by an effort of the will, unless the position of the leg be altered. This is probably a physiological representative of a certain class of muscular spasms which have assumed pathological dimensions.

**Functional Spasm.**—The spasmodic affections which have already been considered owe their origin directly or indirectly to some gross



tangible disease. But there are many cases in which this is not so, and in which the most careful pathological examination by skilled observers reveals nothing. Nor is the spasm under such conditions necessarily short-lived: on the contrary, it may last for months or years. Fine anatomical alterations, no doubt, occur in the nerve structures involved, but we know not what they are. The similarity which exists between the two classes of cases, not only in the manner in which the muscular spasm shews itself but also in its distribution, indicates that the same parts of the nervous system are involved in gross disease and in functional. Clinically the diagnosis between them rests not so much on differences in the character of the muscular spasm, as on considerations of age, sex, the circumstances in which they originated, and the sensory and other phenomena which accompany them. It has been seen what an important part the pyramidal tract, and the centres in the cortex from which it emanates, play in the production of spasm due to gross disease. In most cases it is defective transmission of nervous energy along this tract which indirectly produces spasm by the resulting overactivity of the spinal centres. If, therefore, there were evidence of a similar condition of feebleness on the part of the brain, and of the fibres which travel from it along the cord in functional cases, this would explain the origin of a number of cases of functional spasm. The frequency with which total or partial hemianaesthesia occurs in these cases, involving all the senses, shews that there is deficient nerve power, or neurasthenia, of the whole brain; and great increase of the deep reflexes points to the absence of the normal inhibitory power of the pyramidal tract. In cases of hysterical hemianaesthesia, without any marked loss of power or muscular spasm, it may be shewn that motor power is really deficient on the side affected. In one such instance the right arm could only reach forty-five on the dynamometer scale, while the left reached fifty, the right being the anaesthetic side. Although the striking phenomena, sensory and motor, may appear in these cases to be unilateral, careful examination shews that they are really bilateral, but more marked on one side than on the other. So that it may be asserted that there is a general deficiency of nervous energy in the brain as a whole, although one side or even smaller portions of the organ may be specially affected. And this probably accounts for defects in sensation and in movement, and for the spasm which exists in many of these cases—phenomena which simulate closely those of gross disease of the same parts. The diminished energy in the cells of the motor area of the cortex, and the consequent diminution in the inhibitory or steadying action of the fibres proceeding from them to the spinal motor centres, may be looked upon as the important factor in the production of hysterical paralysis and spasm. This feebleness may extend to the centres in the cord as well, and give rise to the absence of knee-jerk and flaccid paralysis—conditions which are not infrequent in functional disease. In some cases, in fact, there may be deficient nerve power from one end of the nervous system to the other; either generally distributed, or more marked in some centres and nerve

tracts than in others. A girl of sixteen, for instance, lost the use of her left hand for eighteen months. She was a strong healthy girl and free from evident hysterical tendencies. The affection began with swelling and blueness of the fingers, such as is seen in chilblains; the hand was cold and numb, had a swollen puffy look, and was completely paralysed. She recovered suddenly after the application of a blister to the wrist, and then lost power in the left leg, which also suddenly got well.

The so-called "professional hyperkineses" (writers' cramp, histrionic spasm, pianists' cramp, telegraphists' cramp, etc.) admit of a similar explanation: but in them the diminished power in the voluntary motor tract is due to exhaustion from overwork. All the conditions of spasm which occur in cases of gross lesions of the nervous system may be found, more or less accurately reproduced, in functional cases. Exaggeration of the "tendon-phenomena" plays an important part in some of the latter class, just as it has been shewn to do in the former. A healthy girl, aet. sixteen, who had never had an illness, and who had no evident neurotic peculiarities, went out for a row on the Thames with some friends in the summer of 1885. She rowed without interruption for five hours, a very unusual effort. About an hour after returning home her arms "began to twitch," and the movements continued uninterruptedly until I saw her in the following December. Both arms were then the seat of similar and synchronous movements, occurring regularly about 160 times a minute. They consisted of rapid elevation and retraction of the arm at the shoulder, partial flexion at the elbow, and slight extension at the wrist: in fact, they bore a very marked resemblance to the movements of the hands and arms in rowing, the extreme rapidity of the "stroke" making up for the limited extent of the movements. In these rhythmical spasms the slight stretching of the tendons of one set of muscles, produced by the action of their opponents, makes them contract, and they in their turn bring the latter into play.

The condition of the nervous system which gives rise to functional spasm is very ill-defined in its nature; it is, as far as one can judge, a diminution in the nervous energy which specially affects, or is more pronounced in, the higher centres. Hysterical people are those who produce a limited supply of such energy, probably on account of some inherited or acquired anatomical and physiological peculiarities. But the standard of health in different individuals at different times is as variable in the nervous system as it is in other organs; and there are many patients who suffer from muscular spasm, and other symptoms of functional nerve disease, who, under more favourable conditions of life, would have remained free from them; whilst there are others who look almost with scorn upon such sufferers, and who, nevertheless, if subjected to hardship involving stress and strain upon their nervous system, might themselves fall into the category of "hysterical" patients.

It will no doubt have been observed that in the course of the remarks which have been made on "tendon-reflexes" and on "spasm," little or no

reference has been made to the cerebellum. And this is an intentional omission; for I have failed in obtaining at the bedside precise information as to the effect of diseases of this organ upon the phenomena in question. It may be that the cerebellum plays an important part in the production of spasm and in the modification of the tendon-reflexes; but the evidence that this is so does not at present appear to be decisive. It is, therefore, advisable simply to quote Dr. Hughlings Jackson's views on the matter, from the first Hughlings Jackson lecture, delivered before the Neurological Society on 8th December 1897:—"I have now to restate an old hypothesis on dynamical relations of the two sub-systems by inter-mediation of motor centres of the lowest level. Speaking very roughly, and neglecting some parts of the body, the cerebellum represents movements of the skeletal muscles in the order trunk, leg, arm, preponderatingly extensor-wise; the cerebrum represents movements of the same muscles in the order arm, leg, trunk, preponderatingly flexor-wise. It is also supposed that impulses from motor centres of the higher levels of each sub-system continuously act upon the motor centres of the lowest level; that the impulses from each set of higher levels antagonise or inhibit one another in different degrees upon different lowest motor centres; that the degree with which the cerebral and the cerebellar impulses antagonise one another is the same as the order of the degree of their different representations of movements of muscles of the body. In accordance with this hypothesis the rigidity in the common cerebral paralysis, hemiplegia, results because cerebral influence being taken off the lowest motor centres as the cerebrum represents movements in the order arm, leg, trunk, cerebellar influence upon those lowest motor centres is no longer antagonised; there is cerebellar 'influx' into the parts which the cerebrum has abandoned.

"It was asserted against this hypothesis that upon complete transverse lesion of the spinal cord above the lumbar enlargement—both cerebral and cerebellar influence being excluded from motor centres below the lesion—the legs are rigid and the knee-jerks exaggerated. But a few years ago Dr. Charlton Bastian brought forward cases shewing that upon total transverse lesion of the spinal cord above the lumbar enlargement the legs are flaccid and the knee-jerks absent. His conclusions are, I think, adopted by most neurologists in this country; they have been confirmed by Bowlby, Thorburn, and Bruns. I have several times stated the objections which may be brought against the theory of cerebral and cerebellar influx, some of which I admit to be serious.

"There is another way of considering the hypothesis of relations of the cerebral and cerebellar sub-systems to one another by their having the lowest level in common; we may compare and contrast certain cerebral and certain cerebellar maladies with one another as being Complementary Inverses (corresponding opposites). The best-marked complementary inverse is a case of extensive cerebellar paralysis (trunk, legs, arms), and rigidity as the corresponding opposite of the double hemiplegia (arms, legs, trunk), and rigidity of an advanced case of paralysis agitans; in the



former the attitude is opisthotonic, in the latter slightly emprosthotonic. There is another very important complementary inverse; in some cases of tumour of the middle lobe of the cerebellum there are tetanus-like seizures. They, being paroxysmal, are obviously of different nature from the persisting cerebellar paralysis with rigidity just mentioned as certainly as an epileptiform paroxysm (I mean the epilepsy described by Bravais, 1827) is of different nature from hemiplegia with rigidity. These tetanus-like seizures depend, I suppose, on occasional excessive discharges beginning in some part of the cerebellum; such paroxysms are, speaking generally, the complementary inverse of epileptiform or epileptic seizures from sudden occasional excessive discharges beginning in a part of the cerebral cortex. I used to think that drawing back of the neck was especially a cerebellar symptom. Dr. T. Buzzard has, however, published a case of retraction of the head from tumour of one temporo-sphenoidal lobe. Tetanus-like seizures occur in cases of glioma of the pons. I have pointed out that when there is cerebellar tumour such seizures may be said to be owing to pressure on the adjacent corpora quadrigemina or subjacent medulla. Those who adopt the pressure hypothesis have, in some cases of tumour of the middle lobe of the cerebellum, three things to account for: (1) cerebellar paralysis, (2) cerebellar paralysis with rigidity, and (3) tetanus-like seizures."

**Spasm of Involuntary Muscles.**—In defining the meaning of spasm on p. 313 I said:—

"By spasm is meant excessive muscular contraction; and in the case of those muscles which are under the control of the will, excessive contraction is that which occurs in defiance of the will; or which, although beginning as a voluntary act, transgresses the limits which the will would impose upon it. Where involuntary muscles are concerned the definition of excessive is more difficult. When the muscles of the intestine, for instance, make spasmodic efforts to drive along the contents of the bowel through a portion which has been narrowed by disease, so far from the muscular action being excessive, it may be insufficient for the purpose. In such a case, and in others of a similar kind, it can only be said that spasm is muscular contraction which exceeds that which occurs in conditions of health, and in the course of the normal physiological processes."

In ordinary circumstances, between meals, intestinal peristalsis goes on slowly and continuously, as a result of the automatic action of the nerve-cells and -fibres which are found in the wall of the bowel. When food passes along the gut the movements are increased reflexly; and irritating substances may give rise to acute spasm on the part of the muscular coats, whilst chronic obstruction will give rise to chronic spasm with frequently recurring paroxysms of increased severity. Persistent spasm of this kind produces marked muscular hypertrophy, and the wall of the bowel increases in thickness. Such cases may be looked upon as instances of functional spasm. Most cases of visceral spasm are probably



of the functional variety : but the "visceral crises" of locomotor ataxia must be ascribed to gross nerve lesions. The vomiting produced by tumours and other diseases of the brain is another instance of spasm due to a gross lesion ; but the exact way in which the vomiting is brought about is uncertain. Functional spasm of the muscles of the oesophagus gives rise to temporary stricture of this tube, which may disappear after a bougie has been passed once, or oftener. Cramp of the muscles of the limbs may occur in gouty patients, owing probably to the circulation of certain products of abnormal metabolism ; and similar paroxysms of muscular spasm may no doubt affect involuntary muscles. The sphincter ani is occasionally in such subjects the seat of the most painful spasm. Not only in the gastro-intestinal canal does spasm occur, but probably wherever involuntary muscles are found in the body.

The vascular system, for instance, affords us examples. Ergot taken internally, or subcutaneously administered, produces contraction of the muscular coat of the arteries, and even gangrene may result therefrom. In Raynaud's disease spasmodic contraction of the arteries occurs in the stage of "local syncope," and may produce gangrene. Attacks of migraine are often accompanied by evident contraction of the temporal artery, which, as the attack subsides, again becomes softer and larger. There is reason to think that in this disease a similar condition of vascular spasm is present in other organs too ; for during and somewhat preceding the attacks the urine may be much diminished ; and then, as soon as the attack goes off, flows freely again. The inability of the stomach during the attack to digest, or even to absorb fluids which may be present, and the sudden recovery of its power as soon as the attack subsides, are probably due to vascular spasm.

Again in the respiratory system the muscles may overact. The paroxysms of asthma are accompanied by a narrowing of the smaller bronchial tubes, which gives rise to diminished entry of air into the lung and to numberless rhonchi.

In hysteria intense adductor spasm of the vocal cords sometimes occurs, giving rise to dyspnoea and stridor. Even the diaphragm is not exempt from spasm. A very neurotic woman, aged thirty-seven, had for eleven years suffered from periodical attacks in which loud squelching and churning noises were produced within the abdomen, audible at a distance from her. On close examination it was seen that the abdominal movements were produced by jerky spasmodic descents of the diaphragm, and hiccup often accompanied them. There was no evidence of gastro-intestinal distension, and no pain. The woman also suffered from attacks of asthma.

Paroxysms of hepatic and renal colic are probably largely due to the spasmodic contractions of the bile-ducts and gall-bladder in the one case, and of the ureter in the other, which are induced by the presence of a calculus. The same occurs in the case of the urinary bladder when a calculus, enlarged prostate, stricture, or other pathological condition interferes with the easy flow of urine from it.

The uterus, too, another of the hollow muscular organs, may often be the seat of spasm, produced either by local conditions or by the circulation of poisons, such as ergot, through its substance.

The ovaries contain muscular tissue, and it is possible that paroxysmal contractions of this may be responsible for some of the pains and other disturbances which affect these organs.

It appears, therefore, from what has been said, that spasm is not confined to voluntary muscles, but may occur wherever muscle of any kind is found. If the pathology of spasm in voluntary muscle is often obscure, and difficult to explain, it is frequently no less obscure in cases of visceral spasm. But it may be asserted, probably with truth, that in the latter case, as a rule, the pathology is more simple, the overaction of the muscles being often produced by local causes, and then generally reflex in character.

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## MEDICAL OPHTHALMOLOGY

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THE eye is an outpost of the nervous system ; its structures also share in many general changes, and are peculiar in their susceptibility to certain morbid processes, which are revealed in a degree and manner impossible elsewhere. Its function is to receive the waves of light on a structure in which they can excite nerve-impulses. The reception of light involves transparency, and its due arrangement involves refracting media for concentration. The invention of the ophthalmoscope has enabled us to utilise this mechanism in the opposite way, and to view the interior, by the light reflected back from it, magnified as by a powerful lens. By the direct method of examination the fundus is seen magnified fifteen times, and five times by the indirect method. The conditions for observation are thus unique. All the structures that are visible may undergo changes in various diathetic diseases, the vessels and the blood within them may present alterations, and hæmorrhages are seen in the eye sooner than in any other structure. Certain forms of disease of the brain produce alterations within the eye which reveal their presence, and even their character, sometimes before they can be surely discerned in any other way. The movements of the eye and its appendages are of peculiar complexity, and their derangement is often of special significance. Indeed the eyeball may become a pathological microcosm. In this article a systematic outline of its chief indications will be given, avoiding repetition of the points discussed in detail elsewhere.

**ACCESSORY STRUCTURES.**—The **eyebrows** are of little medical significance, and indeed of small importance to man, although the hair-follicles are said to possess a greater degree of tactile sensibility than any similar structures of the body. This is lost in paralysis of the first division of the fifth nerve. The eyebrow reveals, by its position, the state of contraction of the frontalis muscle, and is higher in ptosis, in consequence of its associated overaction.

**EYELIDS.**—**Movements.**—The upper lid is raised by the levator supplied by the third nerve, and also by the unstriated fibres which descend beneath the levator and are inserted into the upper edge of the tarsal cartilage. The latter are supplied by the sympathetic, and the



slight drooping of the lid in paralysis of the sympathetic is ascribed to their inaction. Their overaction is supposed to cause the elevation and hindered descent of the lid in Graves' disease. The upper lid is lowered by the orbicularis palpebrarum, which also raises the lower lid. The contraction of the inner tarsal part of the muscle brings the lids together gently, as in sleep; that of the outer part closes them firmly, with much wrinkling of the skin. Besides these muscles, another agent in moving the lids is the convexity of the eyeball behind the cornea, against which the tarsal cartilage rests. Its influence is greatest when the eyelids are kept in close apposition to the globe by the tone of the orbicularis. It is probably the chief agent in moving the lower lid with the eyeball, when this is moved up or down, and it has also some influence on the upper lid. This I pointed out in 1879, and also that, in isolated paralysis of the inferior rectus, when the eyeball is not moved downwards, the upper lid does not descend in an effort to move the eye—evidence that its descent is due to the actual motion of the globe. The upper lid at once descends if the orbicularis contracts. When the eyeball moves downwards it moves the lower lid down as well as the upper. There is no ability to contract the upper half of the muscle without the lower, which would raise the lower lid. The movements of the eyelids with the globe are thus effected with the eyeball and levator palpebrae superioris. Hence they are not impaired in facial paralysis, except in a very slight degree, in consequence of the diminished tone of the orbicularis, which lessens the approximation of the muscle to the tarsal cartilages.

The retraction and tardy descent of the upper lid in Graves' disease seems to transcend the normal power of the unstriated muscular fibres under normal conditions, so far as this can be guessed at. But it is conceivable that they may become hypertrophied from constant overaction. The symptom is described in the account of that malady (Vol. IV. Part I. p. 367), but it is occasionally met with quite apart from that disease. In a married woman of thirty it came on, after a period of great anxiety, in one eye only. It continued for a year, and then passed away. In another case, a girl of seventeen, it was associated with a peculiar subcutaneous state in the upper part of the trunk, like myxoedema, which caused slight bulging of the eyelids. Her after-history is not known. A somewhat similar symptom, in which the upper lid is not only tardy in descent in looking down but also hasty in ascent on looking up, has been described in an isolated form as "pseudo-Græfe's" symptom.

**Paralysis.**—The orbicularis is, of course, paralysed in any disease of the facial nerve or centre. When this is incomplete the muscle suffers much or little according to the damage to the fibres of the nerve. It is weakened in some cases of degenerative ophthalmoplegia externa, and hence it has been thought that the fibres for the orbicularis arise from part of the oculomotor nucleus, and descend the pons to join the rest of the nerve. But in most cases of the kind the muscle does not suffer,

and it escapes in acute inflammation of the nucleus. Association in function or in pathological susceptibility does not necessarily imply central proximity. Weakness of the orbicularis is conspicuous in some cases of primary myopathy, especially of the Landouzy-Dejerine type, without failure of the ocular muscles, and it is also frequent, often with such failure, in the mysterious malady "myasthenia."

In facial paralysis, when an effort is made to close the lids, the eyeball rolls upwards and outwards, a movement which is clearly due to a normal association, for it occurs apart from paralysis, carrying the cornea partially under the rim of the orbit, and it is further protected by the much-ruffled integument. In a few persons there seems to be, instead, a like association with the inferior rectus, for the eyeball turns downwards instead of upwards. The orbiculares are bilateral muscles which usually act together and are incapable of completely isolated contraction. They are bilateral in their central representation in greater degree, for instance, than the zygomatics. Hence, in cerebral hemiplegia the paralysis of the latter is greater than that of the orbicularis, but it may be considerably affected by an irritating cortical lesion, such as meningitis. The mechanism is not quite clear.

*Ptosis*.—Paralysis of the levator palpebrae superioris is described in connexion with the third nerve, but some additional points may be mentioned. The muscle is paralysed alone when the branch to it suffers; when the trunk of the third nerve is affected, the fibres for the superior rectus commonly also suffer, and this is true in nuclear disease. The roots and cells for the two muscles are in proximity, subserving associated action. In a case of left hemiplegia, due to an area of softening in the right crus, the two muscles were paralysed on this side, and there was degeneration of the posterior roots of the right third nerve (Kahler and Pick). The centres must, however, be distinct, since 2 cases have been observed of paralysis of the superior rectus without any paralysis of the levator, from a focal lesion. In each there was left hemianaesthesia, and in one also considerable left hemiplegia (Kahler, Wilbrand and Saenger).

The overaction of the frontalis which accompanies ptosis, with elevated eyebrow and more wrinkled forehead, suggests an effort to raise the eyelid by traction of the skin, which has indeed a trifling effect on the lid. But the overaction is due to the normal association of the frontalis, levator, and superior rectus, as seen in the act of looking up. This is arranged in the nerve centres, and is shared by the occipitalis. In the combination the superior rectus leads, and is followed by the others. If the levator is paralysed, the frontalis overacts (in the same way as an ocular muscle in "secondary deviation"); the superior rectus does not. If the frontalis acts primarily, its action does not involve the levator any more than that of the levator involves the superior rectus.

The levator often suffers first, and seldom escapes, in nuclear palsy of the ocular muscles, especially such as is met with in tabes. Ptosis may occur and pass off in this malady, but tends to recur. It is often unilateral, at least in considerable degree. The superior rectus is usually

also affected, always when the cause is a true syphilitic lesion of the nerve. Ptosis is also, as a rule, the first symptom of a peculiar atrophic form of external ophthalmoplegia which may begin at any time of life, and has a slowly progressive course, interrupted by stationary periods. It has been observed in both sexes, and in many members of the same family. In one instance nine persons suffered in two generations. Hence juvenile and family forms have been distinguished, but the symptoms are essentially the same in all; a distinctive characteristic being the escape of the internal ocular muscles. Isolated paralysis of the levator from cortical disease has been described in rare cases, but the few instances in which the position of the lesion has been ascertained are not consistent. A majority point to the posterior part of the parietal lobe. Its condition must depend on the state of the brain, and especially of the visual region in the sleeping and waking states. The fact that its isolated paralysis may occur, shews that its association with the ocular movements is chiefly of subsidiary arrangement.

The slight ptosis that results from paralysis of the sympathetic has been already mentioned. The plain muscular fibres, to which it is ascribed, do not seem to take any part in the voluntary elevation of the lid, but their tone may reinforce that of the levator. They are said to be relaxed only during sleep, and from this, in facial paralysis, the eyelids come together more completely during sleep than in the waking state.

In myasthenia, in which weakness of the orbiculares is so common, ptosis is also frequent in association with defect in the upper movement of the eyeballs, although the two are not proportioned in degree. I have seen a case in which the lid of each eye habitually covered a third only of the cornea and could not be raised higher, and yet, under interest or surprise, it ascended so as to expose the sclerotic above the cornea. This is difficult to explain, unless there was hypertrophy of the unstriated levator, and it was responsive to emotion. In another rare form of ptosis, which has been described chiefly in women, the drooping develops gradually, but is ultimately considerable and equal in the two lids, with overaction of the frontales. The peculiar feature is, that there is atrophy of all the subcutaneous tissues, so that the lid becomes almost translucent, and the wasting under the edge of the orbit makes the drooped lid appear as if tucked in beneath the bone.

*Functional Ptosis*—"Hysterical Ptosis."—The term has been misapplied to a condition in which the eyelid, usually on one side, is kept down by a gentle contraction of the tarsal orbicularis; the contraction is usually inconspicuous, but at once becomes energetic and obtrusive if the patient is made to look up with the other eye.

The term "Matutinal Ptosis" seems applicable to a form of bilateral functional drooping of the lids common in conditions of nervous weakness. Their state during sleep persists, for a time, after waking. The patient finds it impossible to open the eyes until after an hour or two, though the lids are not adherent from the effect of secretion. The return of power is gradual, and may be quickened by any painful



application to the temples—a liniment or electricity. The symptom passes away as the patient gains strength.

*Inhibitory Ptosis.*—The power of the levator may be temporarily diminished by severe neighbouring pain. Partial drooping of the lid may attend the pain of migraine, when severe, and is on the same side. It passes off soon after the pain. It may also result from irritation of the fifth nerve. It has followed division of the fibres of the nerve, and has resulted from the extraction of a decayed upper molar tooth; the ptosis came on some hours later, and was attended by frequent attacks of clonic spasm of the levator, each lasting a few seconds; both symptoms gradually subsided, and had disappeared by the fifth day.

*Congenital ptosis*, when not due to a malformation of the lid, is usually bilateral and partial, but sometimes exists on one side only. It is probably due to an imperfection in the nerve centres. It may be hereditary, and sometimes affects several members of a family, occasionally only the females. An abiotrophic form has been described coming on after puberty; it may be ascribed to local vital failure. Each form is attended by an overaction of the frontalis; the elevation of the eyebrows may even be more conspicuous than the slight drooping of the lids, and it causes an aspect of habitual distress. In other slight cases a sleepy expression results. Occasionally the ptosis can rarely be noticed until the patient tries to look upward. The superior rectus is sometimes normal, but more often its action is also absent. In the rare cases in which congenital ptosis is unilateral, it is often combined with a difference in the height of the eyeballs and ocular fissures; there may also be an abnormality in the action of other muscles supplied by the third nerve, but never, it is said, in the external rectus. The position of the upper lid may not correspond with the defect of power; it sometimes droops very little, when there is no power of raising it, apparently from the condition of the structures which replace the muscle. In the few cases of congenital ptosis in which the state of the centres has been ascertained, an absence of some of the cells in the oculomotor nucleus has been described, but their locality in the nucleus has not been the same in the various cases.

The sensibility of the eyelids depends on the fifth nerve, and is great, in accordance with their important function of protecting the delicate organ of vision. The nerve structures subserving it seem to possess a correspondingly greater power of vital resistance. In cases of tabes, in which universal analgesia involves the face, I have repeatedly found that the sensitiveness to pain is preserved over the eyelids, near their margins, in a zone of variable width, as it also is on the inner edge of the nostrils, and around the lips.

The *palpebral reflex* is a contraction of the orbicularis caused by a sudden visual sensation or by touching the cornea or conjunctiva. Hence two reflexes are distinguished, the optic and the fifth nerve reflex. They are similar in character, varying according to the character and strength of the excitant. They are necessarily lost in paralysis of the orbicularis.



The optic reflex depends more on the suddenness than on the strength of the stimulus. It is convenient as a means of ascertaining the existence of sensitiveness to light when it cannot be ascertained otherwise. If light is thrown into the eye, first from one side and then from the other, the absence of this reflex may shew the presence of hemianopsia, in a patient who is unconscious or aphasic, more usefully than the pupil-reflex. For the same purpose we may employ what may be termed the *visual reflex*. If an object, such as the finger, is suddenly brought near the eye from one side, the reflex action is due to the perception of the proximity of the object, and involves a higher cerebral process than the effect of the mere flash of light.

*The conjunctival reflex*, excited through the fifth nerve by touching the conjunctiva or cornea, is increased when these structures are inflamed. It is abolished by disease of the fifth nerve, and its ready access makes it the most convenient guide to the influence of anaesthetics on the nerve centres. It should be noted that the conjunctiva over the sclerotic is not very sensitive to a gentle touch, but more so to an object that is cold than to one that is correspondingly warm. The same reflex is readily elicited by a touch on the eyelashes; the "ciliary reflex" it may be termed. In a perfectly blind eye the reflex is said to be produced, in conjunctival inflammation, by light falling on the eye. The point needs more confirmation, but it is conceivable that disturbed nerve-elements may become sensitive to the rapid vibrations of light, as they are normally to the slower vibrations of heat. In the hemianaesthesia of hysteria, when the conjunctiva seems insensitive, the conjunctival reflex, though not lost, is distinctly less than on the other side, and is in marked contrast to the unaltered pupil-reflex.

**Spasm of the Eyelids.**—Contraction of the orbiculares, "blepharospasm," occurs in painful affections of the eye and conjunctiva, and is often intense in early life. Facial spasm, clonic and briefly tonic, often begins in the eyelids, and may be bilateral in them and not elsewhere. The orbicularis shares the contracture, often with clonic movements, that follows severe facial neuritis, and causes the ocular fissure to be habitually a little narrower than on the other side, and to close unduly in smiling. The zygomatic muscles contract too much when the eyelids are closed. The frontalis never shares the overaction. Its cause is not known. It curiously simulates a diffusion of the impulse in the nerve, but its cause must be higher, since the damage to the nerve does not explain the persistent contracture. It has been ascribed to muscular changes, but these do not explain the associated overaction or the clonic contractions. It is more probably due to a morbid state of the nucleus; its function may be deranged in a peculiar way by the long cessation of the afferent impulses from the muscles, normally produced by their voluntary action—impulses which reach it through a separate nerve, the fifth. It is of some practical importance, because its appearance shews that most of the possible improvement has been attained, and that treatment, such as electricity, which stimulates the sensory nerves, and so tends to augment

reflex spasm, should be stopped. It is well to warn the patient of its advent, or he may think it indicates a return of the original morbid state.

Epileptic convulsions, especially when unilateral, may begin in the orbicularis by clonic spasm, which spreads thence. The muscle on the other side usually, but not always, shares the spasm in slighter degree. I have known such fits, when much lessened in degree, to be limited to the orbicularis. In one case no other muscles were affected; in another, there was simultaneous spasm in some muscles of the eyeball.

**EYEBALL.—Nutrition.**—The eyeball presents the most delicate example in the body of the relation of nutrition to the nerves. The cornea is extra-vascular, being dependent for its nutrition on the plasma from the vessels around its circumference. Its nutrition is therefore deranged with extreme readiness, and its transparency and smoothness cause the least disturbance to be revealed. With the rest of the eyeball the cornea depends for its sensitiveness on the fifth nerve. By this its nutrition is influenced, as is that of all superficial structures of the body, by the sensory nerve-fibres. The more is known of the tissues and nerves, the less room can be perceived for the conception of special trophic nerves or centres. The nutrition of the tissues (except the muscles) seems to be determined by the nutritional state of the fibres connected with the posterior spinal roots; their endings are in direct contact with the tissues, and these are influenced by the nutritional state of the nerves, communicated by contiguity, and the mysterious influence which passes, by all that contact involves, from a higher tissue to a lower. This seems the essential element in the control of nutrition by the nervous system. Yet the tissues have an independent vitality so far as their structural elements are concerned, and their nutrition, once set wrong, may have an independent course maintaining and often augmenting the derangement. The lesson is instructively taught by the eyeball.

The nutritional state of the fibres of the fifth nerve depends on the cells of the Gasserian ganglion. The fibres beyond it rapidly degenerate if separated from the ganglion by disease, or if this is destroyed. This degeneration usually entails keratitis and ulceration. Disease behind the ganglion has not this effect unless it is so intensely irritant in character as to spread to the cells and affect the fibres beyond. The effects of removal of the Gasserian ganglion for neuralgia have clearly shewn the nature of the relation of nutrition to the nerves. Were the removal not aseptic, there would doubtless be inevitable destructive inflammation of the eye. When all infective influences are prevented, it is still found difficult to avoid slight changes in the cornea during the first week. They are found to be excited by the irritation of particles of dust, etc., reaching the eye. If this be effectively prevented by securing the eyelids together with a few stitches, during the first week, the danger is almost entirely obviated. After the first week or ten days it has ceased. The cornea is still insensitive, but it may be exposed with the same impunity as that of a normal eye. The cornea is only unstable in its

nutrition during the active process of degeneration of the nerve-fibres. When this process is over, so is the danger to the cornea. But should the nutrition of this be disturbed, however slightly, it is apt to progress independently, and may have grave results. Facial paralysis, with inability to protect the eye from dust, or to remove it by the motion of the lids, may cause conjunctivitis, but not inflammation of the cornea, nor does it ever result from the exposure of the eye in Graves' disease. A peculiar bacillus is to be found in the ulcerated cornea, no doubt of secondary relation (Davies and Hall).

*Sympathetic ophthalmitis* was formerly regarded as a disturbance of nutrition due to a deranged nervous influence induced by symmetrical "sympathy." This explanation is now generally regarded as untenable. The facts, carefully scrutinised, seem to suggest a direct passage of pathogenetic material from one eye to the other, material probably organismal. It has, in rare cases, been seen to commence in the optic papilla, but other parts of the eye are more susceptible to the morbid agency, and a similar structure to that in which the agent was produced may afford a soil more suitable than other parts present. In this sense only the affection can be regarded as "sympathetic."

**Movements of the Eyeball.**—The external muscles are supplied by the third, fourth, and sixth nerves, and the symptoms of their paralysis are described in the article on the cranial nerves. Only some other points need be here mentioned.

*Congenital anomalies* are not rare, and become important in disease which might cause impairment of the ocular movements. The eyeball and ocular fissure are often slightly higher on one side than on the other, and the difference is preserved in all movements of the globe. This only needs to be recognised to prevent error. Another difference, which is common, is that the extreme upward movement of the eyeball is a little greater on the one side than on the other. At the maximum there is a distinct difference in the level of the lower edge of the cornea, although there is none in the mid-position; it may amount to a twelfth of an inch. In a case with symptoms of impairment of other cranial nerves this natural difference may be mistaken for a morbid symptom.

An irregularity in the movement of one eye is also occasionally met with. A movement, which should be straight, is oblique, and brings the eye out of correspondence with the other. Such a defect may be very puzzling if it occurs in a patient who has cerebral symptoms, for instance, optic neuritis, or other signs of intracranial disease. One important indication generally enables the nature of the abnormality to be recognised. No diplopia can be found in these cases of defect of correspondence in the position of the two eyes, when congenital or from early life, whereas it is always to be ascertained, by a coloured glass, when the defect is of recent origin. The slight inequality in the height of the eyes, just mentioned, often attends this anomaly of movement.

**Reflex Fixation.**—When an infant begins to follow a light it is probably in consequence of the development of a reflex process of fixation,



by which the muscles maintain the eyeball in a position that permits the image of the light to fall on the most sensitive part of the retina. The reflex centre is probably in the mid-brain. Very rarely this process is revealed by a dissociation from the connected movement of the head, by which it is normally moved towards the object that is fixed, and the work of the ocular muscles is lessened. In this dissociation, if the patient is looking at an object, for instance, on the left side, and is told to look at one on the right, he instantly moves his head to the right but the eyes remain fixed to the left, and are only slowly moved into the new position. This has been described in paralysis agitans, and I have seen it in chronic spinal muscular atrophy. Apparently the reflex process has lost its due subordination to the volitional centre.

The conjugate deviation and other disorders of associated movements are described in the section on the Cranial Nerves (p. 516).

**Nystagmus** is an oscillation of one or commonly of both eyeballs, due to an alternating activity of the opposing muscles. The movement is regular or irregular. Some would restrict the name to the regular oscillations, distinguishing as "nystagmoid" those that are irregular. But it is usual to call all forms nystagmus, and it is doubtful if the distinction can be justified by pathological considerations.

An important difference exists between an early form, which appears during the first year of life, and that which comes on later, as a result of disease. The early form is met with when there is interference with vision from any cause, and also in albinos, when an excess of light enters the eye. It also occurs in infants in association with nodding movements of the head. In the early form the motion of the eyes is continuous, persisting when the eyeballs should be at rest in the mid-position. The movement is horizontal, and, moreover, is equal in rate to and fro. The latter acquired form results, as a rule, from central disease; it commonly only occurs on voluntary movement of the eyes, and is not equal in each direction. It is quicker in the direction of volition, and slower in return. It usually ceases when the eye is at rest, in the mid-position, but not always; even then, however, it is quicker towards one side than the other. Its rate varies from 80 to 200 per minute.

The early form is clearly an alternate and equal contraction of the opposing muscles. When voluntary power develops, the nystagmus presents the same quicker character, in the direction of volitional movement, as is seen in the later form. Its development coincides with that of the tendency to fix and follow a light. It apparently depends on an imperfection in the reflex action of the eye, in the due contraction of the opponent muscles, necessary to keep the eyeball steady. Instead of a duly related contraction, the muscles contract alternately from disordered action in the mid-brain centres. When associated with nodding movements of the head, it would seem that the same imperfection is wider in extent. Whether in such cases the head or the eyes lead the way we do not know. When the eyes alone are affected we can conceive that a certain amount of light is necessary for the due development of the reflex



action, and that when this is deficient or excessive, disorder may arise, although we are still unable to explain how it does so. Sometimes the disorder disappears as infancy passes into childhood; sometimes it persists, especially in cases of albinism. The nodding form usually ceases, together with the movement of the head. Allied to it, however, is a malady which has been met with in several members of the same family, in which nystagmus is associated with similar movements in other parts, which persist. It has been called "myoclonic nystagmus" (Lenoble).

The acquired form, which results from disease, as already stated, generally attends movement of the eyes; the movement is quicker in the direction of voluntary motion, and is described as at rest in the direction of the quicker motion. Sometimes, but not often, it occurs in the mid-position. It may attend all movements, but in the upward and downward direction it is small in range. In lateral movements it is usually greater in the eye that moves outwards, and may be confined to this eye. Convergent nystagmus is less frequent. The symptom is seldom combined with defective power, and this is evidently not its cause, for it is often present when there is no defect and always absent with complete loss of voluntary power. It usually goes on as long as the voluntary movement is maintained, equally or irregularly; sometimes the eyes gradually come to rest after a few lessening oscillations. In other cases the movement is rhythmically unequal, two or three slight movements separating each considerable oscillation. Although the motion is usually in the direction of volition, this may not be so in oblique movements; in these it is in some cases horizontal, in some vertical, one or other of the components determining the direction. A more striking feature is presented by cases in which nystagmus in one horizontal direction dominates the movement. For instance, a patient with insular sclerosis presented wide and regular horizontal movements, quick to the right; this continued to the mid-position, and even on movement to the left, only ceasing when the eyes were half-way to the left canthus. Beyond this, the nystagmus was to the left. On looking up or down the horizontal nystagmus continued. Nystagmus may be rotatory, and this is often in one eye only, usually with a downward movement of the outer part of the eyeball. It is evidently due to the oblique muscles, but, strange to say, is more often seen in lateral than in vertical motion, though in the latter the oblique muscles take more part. In rare cases, the upper eyelid has been observed to move in nystagmus synchronously with the eyeball, not by a communicated motion, but by contraction of the levator.

Nystagmus has been occasionally met with as a normal peculiarity in a few individuals, occurring in sustained fixation on an object, near or distant, or on strong convergence. It has also been described in some cases of hysteria and other functional neuroses, but some doubt may be entertained regarding the nature of these cases. A lateral oscillation of the eyeballs, combined with jerking contractions of the orbicularis, when an effort is made by another person to separate the closed lids, has been

described in 3 per cent of normal persons. It has been called "associated nystagmus," but seems of small importance. With these exceptions, and that of miners (p. 338), together with a rare labyrinthine form, nystagmus is the result of organic disease in the neighbourhood of the mid-brain or the cerebellum. Usually the disease is visible, less commonly it needs the microscope for its detection. The symptom is common in Friedreich's ataxia, although rare in ordinary tabes or in tabetic general paralysis. In disseminated sclerosis it is extremely common, probably in consequence of islets of sclerosis in this part. It is a frequent symptom of tumours of the cerebellum, pons, or near the corpora quadrigemina, and also of foci or softening in these parts. For instance, an area of softening in one-half of the pons, abolishing all movement of the eyes towards that side, may cause extreme nystagmus on movement towards the opposite side. But it is hardly known in disease of the cerebral hemispheres unless this is so placed as to interfere with the mid-brain, but a very slow spontaneous oscillation of the globe has been described in the early stage of extensive lesions of the hemisphere, especially with conjugate deviation of the eyes (Souques). I have once seen it in softening of the optic thalami.

Labyrinthine disease is an instructive but infrequent cause. When the tympanic membrane is ruptured, pressure on the orifice of the meatus will sometimes cause nystagmus towards that side. This was carefully observed by Hirschfeld in a case in which the ossicles also were destroyed; increase of aerial pressure caused nystagmus towards that side, whilst diminution of pressure caused similar movements towards the opposite side. One case under my care, which ultimately, from its perfect recovery, seemed to be purely labyrinthine in nature, was thought at first to be cerebellar, and caused continuous convergent nystagmus. Rotation of the body, as on a revolving stool, causes brief nystagmus, probably through the labyrinth. The resulting motion of the eyes is quicker towards the side opposite to that to which the rotation is.

*Pathology.*—The only attempt to explain the nature of nystagmus is that of Wilbrand, who regarded it as due to derangement of the voluntary impulse or of the general reflex centre for the eyeballs, so that there is defect of harmony between the two. But this scarcely explains the peculiar oscillation of the globes. In all muscular movements, including that of the eyes, steadiness depends on the perfect adjustment of the acting muscles and of their opponents; the latter yield and yet give due support. In nystagmus, the acting muscles suddenly relax and their opponents contract, to cease in turn, and the process goes on. Important light on the mechanism of this alternation may be obtained from the researches of Prof. Sherrington. He found that in animals, if the spinal cord is divided in the cervical region, so as to cut off the voluntary impulse from the lumbar centres, these pass into a peculiar functional state. When contraction is excited in a group of muscles, say the extensors of the knee moving the leg, their action ceases suddenly, and a contraction of their opponents occurs, to cease in its turn when the

extensors again contract. Thus there develops an alternate contraction of the two sets, which goes on automatically. If the nerve to the opponents be divided and the proximal end stimulated, the effect is at once to inhibit the centre for the acting muscles. Since the nerve is purely muscular, the inhibition must be due to an impulse from the opponents caused by their extension, doubtless through the agency of the muscle-spindles, and it also causes their own contraction. This process goes on alternately by a muscle-reflex action. Symptoms of the same nature may be occasionally observed in cases of lateral sclerosis in man.

The resemblance of this automatic alternation to nystagmus is so close as to suggest that the same process must underlie both; that nystagmus is also due to a muscle-reflex mechanism. Whether definite muscle-spindles do or do not exist in the ocular muscles (Dr. F. Buzzard has found a structure resembling them), we cannot doubt that afferent impulses arise in the muscles, because each muscle-nerve gives a branch to the fifth. A centre must exist in or near the mid-brain, analogous to the spinal centres, which subserves binocular combination and reflex action. Nystagmus does not arise, as a rule, from disease of the cerebral hemisphere, and cannot therefore be due to defect of the volitional impulse. Its causes are in the mid-brain, pons, and cerebellum, and must act by deranging the influences that act on the mid-brain ocular centre. When its balance is thus disturbed, the muscle-reflex action becomes insubordinate, and its alternate activity is actually evoked by the volitional impulse. The light-reflex must be through the same centre so far as the muscles are concerned. During the first month of infancy, when fixation is developing, an habitual defect or excess of light may induce persistent nystagmus, that is, alternate action of the opposing muscles. This shews how readily the structural arrangements for this may become functionally dominant, and makes its frequency in disease less surprising. So also does the production of labyrinthine nystagmus by causes (rotation, increased pressure, etc.) which disturb the centre for equilibrium, with which the ocular centres are closely connected.

The disturbance may only shew itself when the centre is energised by the will, and the motion is quicker in the direction of volition. After a time, if the process increases, the nystagmus may persist during rest, always in the direction in which it is quicker, and it may even continue in opposition to the will. For example, a horizontal nystagmus to the right may not only continue during vertical movements but also during half the movement to the left. The slight and partial degrees are thus equally intelligible. So is its occasional association with partial loss of power, which must lessen the afferent impulses from the muscle, and so disturb the centre. Wilbrand's explanation of nystagmus approached near to that here advocated; he regarded it as due to a derangement of the common reflex centre or of the volitional impulse, so that there is a want of harmony between the two.

Nystagmus is of great diagnostic service as evidence of organic disease, in which term microscopical degenerations are included. It indicates



disease in the structures related to the ocular muscle-reflex centre. In equivocal cases, especially of disseminated sclerosis, so often thought at first to be due to hysteria, it is often decisive, but it is not alone of much localising value. To this significance of acquired nystagmus as evidence of structural disease, there is an apparent exception in labyrinthine affections, and there is a real exception in a variety that stands alone, and has been left to the last—that of miners.

*Miners' nystagmus* occurs in those who have worked long in ill-lighted coal-mines, in unnatural positions, lying on the back with the head turned to one side, and the eyes directed more or less obliquely. Its incidence is probably facilitated by intemperance, bad air, and the like. The nystagmus that arises is often rotatory and may occur whenever the eyes are in use, or only when they are directed as they are in work. The sufferer is usually conscious of apparent motion of objects, and the spontaneous "dancing" of all he sees is peculiarly disabling.

*Symptoms.*—The early form, which develops in infancy, is not attended by any apparent movement of the objects seen. In the acquired form, due to disease, objects may appear steady, especially when the motion is fine and frequent. Often they are described as moving in the plane in which the eye moves. This is usually the case when the motion is wide in range. Sometimes the patient is conscious of objective movement only during the quick movement, and not during the slow return, and this has been adduced as evidence of the part played by the consciousness of voluntary innervation in determining the sense of movements in objects. But the apparent anomaly that the objects may seem still, when the image is flitting to and fro on the retina, is intelligible if it is realised that all that is ever perceived is a tendency to motion rather than any actual movement. This may be perceived from the nearest approximation we can make to nystagmus. We cannot cause involuntary oscillation of the eyes, which alone would be strictly to the point, but we may oscillate our eyes laterally, to and fro, with some rapidity; the only difference from involuntary oscillation is that there should be more sense of movement in the volitional imitation. But there is hardly any perceptible change of position in a conspicuous object. Generally the impression is of a tendency to move in the opposite direction to the eyes. Only when this movement of the eyes is very rapid does it seem to be in the same direction. I think this is due to the fact that, with the rapid motion, an after-image is left which disappears in the direction of the movement of the eyes. We may thus understand the seeming anomalous answers given by patients about the effect on vision.

**OPHTHALMOSCOPIC CHANGES.**—For the reasons stated at the beginning of the article, the changes in the structures within the eye, visible with the ophthalmoscope, are of great medical importance. Alterations in the media may be of significance, but those of most importance are in the structures at the back of the eye, the fundus oculi, in the



retina, the choroid, the entrance of the optic nerve, and the retinal vessels. Familiarity with the normal aspect of these, and with the variations that are met with in health, is essential for the recognition of pathological changes, but must here be assumed. So also must the knowledge of some congenital anomalies that may be mistaken for disease, such as the white areas near the disc, due to some nerve-fibres having retained for a space their white substance.

**Vessels.**—The double red line that we call a vessel is merely the column of blood within it. The line is double, because the middle of the convexity reflects the light, and where the surface has a sloping curve the tint is much darker. The walls are invisible, except on and near the disc, where they may sometimes be seen as a white line along each side of the red column, chiefly beside an artery. These white lines vary much in extent in different persons, and may sometimes be seen on the disc even in early life; they are increased in width, and extend farther along the vessels in conditions that entail arterial degeneration. There may be another indication of such thickening of the arterial wall in the evident compression of a vein where an artery crosses it. But it is extremely rare for the change in the wall to conceal the column of blood in the vessel, and then chiefly in isolated tracts in cases of Bright's disease, in which the arteries are often narrowed. Reduction in size is extreme in cases of embolism of the central artery; the branches may be reduced to thread-like dimensions. They are also diminished in size when there is any cause of compression of the central artery, as papillitis. The same influence causes the veins to be at first distended. Local enlargement of the retinal arteries is occasionally met with in arterial degeneration, and in Bright's disease distinct fusiform aneurysms have been seen. They are very rare, but aneurysmal dilatations of the retinal capillaries are frequently found with the microscope, in cases in which haemorrhages are common.

In *thrombosis* of the central vein, its branches lose their bright reflexion and are enormously distended, and the retina is usually crammed with extravasations. It may be important as shewing the nature of a vascular lesion elsewhere, and is met with especially in gouty subjects.

*Embolism* of the central artery is usually a consequence of mitral disease, and has occurred simultaneously with embolism of the middle cerebral artery on the same side. The plug is arrested behind the eye, and the sudden stoppage of the circulation causes instant loss of sight, sometimes afterwards regained in part of the retina, if the arrest of the blood is incomplete. The substance of the retina becomes opaque, but the opacity usually spares the macular region, which appears by contrast a bright red. Ultimately a condition of atrophy of the nerve results. Symptoms like those of embolism are perhaps sometimes due to an extravasation around the artery, and also to a retrobulbar thrombosis within it.

*Pulsation* in the retinal arteries may often be seen when the wave is increased in amplitude, as in aortic regurgitation, or the tone of the walls

is low, as in anaemia. But it is more frequently conspicuous in the retinal vein, and appears whenever the artery and vein are in juxtaposition within the sclerotic ring. The distension of the artery compresses the vein, and hinders the flow within it; the diastole in the retinal vein thus coincides with that in the artery, and is greater, the thinner venous wall yielding more readily. Both the arterial and venous pulses are best seen on the optic disc; they may be increased, or brought out in health, by slight pressure on the eyeball; possibly the slight increase in the tension increases the systolic contraction more than it lessens the diastolic swelling of the vessels.

*Spasm of the retinal artery* has probably never been seen, but seems sometimes to occur. It is the most likely cause of cases of recurring loss of sight, in one eye only, lasting a few minutes. Several cases of the kind have been described. In a woman the sight of the right eye was lost for four minutes about once a fortnight; the loss came on and passed away with a dimness, as if a lace veil were in front of the eye, attended by a strange feeling of rotation at the back of the eyeball. In some cases an attack has lasted longer, indeed so long as to transcend nutritional power, with permanent impairment of vision. The fact that the failure of vision was certainly in one eye only, and the ocular sensation which attended it, made this cause the only conceivable explanation.

**The Optic Nerve.**—The entrance of the optic nerve into the eye, through the opening in the sclerotic and choroid, is the most conspicuous object on ophthalmoscopic scrutiny. The fibres spread out on to the retina, rising a little in doing so; hence the term “papilla” is often applied to the disc. They are so transparent as not to obscure the sharp edge of the opening, and their separation leaves a depression or “cup” in the middle part of the disc. Few fibres pass directly outwards towards the macula; hence the cup often shelves on that side to the margin of the disc, and it may be so large as to expose the lamina cribrosa. In other cases the cup is small. The part occupied by the nerve-fibres is rosy, or even red, from capillary vessels, and the normal variations in tint are so great as to be a fertile source of error. When the outer part is the same tint as the adjacent choroid, the disc is readily thought to be inflamed, although careful observation shews the edge to be quite sharp and the disc normal. The central excavation is usually free from vessels, and when it is large the nerve-fibres may be limited to a narrow zone near the edge.

*Inflammation.*—The term “optic neuritis” is usually restricted to the process visible in the intra-ocular end of the nerve, to which “papillitis” is also applied. Any state that can be called simple “congestion,” that is, morbid increased vascularity only, is of doubtful existence, except as a diagnostic pitfall. A normally red disc is constantly said to be congested, when it has no more significance than a rosy cheek. Any definitely morbid state is attended by blurring of the edge from swelling of the structures passing over it, and the edge is more obscured to the direct than to the indirect method of examination, because obscuring

tissue is brought into more precise focus. The swelling soon becomes measurable, encroaches on the central cup, and is attended with the appearance of many minute vessels. The veins are raised on the convexity, and lose their central reflexion as they pass up and down the slope of the elevated papilla to the retina, and, as it increases, they may be dimmed by bending into the obscuring tissue. The arteries share these changes, but in rather less degree, on account of their firmer walls. As the neuritis becomes greater, the central cup ceases to be visible, although a central depression can be recognised by the displacement of the curving vessels, perceived on moving the lens or mirror. The swollen papilla may attain a height of 6 or 8 diopters, and as it increases in height it does so also in width, often becoming two or three times the diameter of the normal disc. It may displace the retina, throwing it into folds concentric with the disc, and sometimes the resulting changes and oedema may produce white spots of degeneration towards the macula. Before this the veins become greatly distended, and haemorrhages appear on the substance of the swelling and in the adjacent retina. This evidence of hindrance to the return of blood has led the stage to be termed "choked disc," and the obstruction has been ascribed to the sclerotic ring; but it is always found to be produced within the swollen papilla, where the veins are seen to be compressed by the inflammatory products and accumulations of leucocyte-like cells. These may be visible as white patches on the surface during life. The swelling may even be so great that its edges overlap the base, in a "fungiform" manner, and the vessels are concealed, reappearing to one side of their position on the edge. This description applies to the most intense and acute forms, which reach their height in a few months or less. Often the swelling is slow and moderate; its substance has a soft woolly aspect, without signs of "strangulation," and it may present little change of aspect during months of observation. In some forms the amount of change may be trifling, and only enough to obscure the edges of the disc and cause slight swelling with very little increased vascularity. This is the case when a retrobulbar neuritis just reaches the eye, and becomes visible there. In all forms, when a certain degree is attained, slight but more often considerable subsidence occurs. When slight, the disc may resume its normal aspect; when considerable the veins and arteries lessen in size, the vascularity of the swelling gradually diminishes as it recedes, until a pale soft-edged prominence is left, which passes gradually into consecutive or papillitic atrophy (*vide* p. 342).

The effects of optic neuritis on vision vary much. The slighter slow form may exist for a long time with little impairment of sight, and in the acute form vision may not suffer until a considerable degree is attained, but then it suffers rapidly, and the failure increases during the stage of subsidence. The field is impaired irregularly, but the blind spot is always increased in size according to the neuritic swelling. It is important to note if the visible neuritis is sufficient to account for the failure of sight.



**Causes.**—Intra-ocular neuritis may be due to blood-states, as Bright's disease (in which it may vastly transcend the affection of the retina), in lead-poisoning with encephalopathy, and in rare cases of chlorosis. It has been met with in some cases of myelitis, apparently as a coincident effect of the blood-state. Its great cause is intracranial disease, especially tumour (to which most of the intense forms are due), abscess, meningitis, particularly of the base; and caries of the adjacent bone. The precise mechanism by which the neuritis is produced is still undetermined. Increased intracranial pressure is certainly an intensifying cause, for when this is relieved by trephining, although the tumour has not been removed, the neuritis ceases to increase and almost always subsides. Moreover, when there is increased pressure, the sheath of the optic nerve is nearly always distended, forming a pyriform swelling behind the globe. But that it is not the sole cause is shewn by the frequency with which large tumours of the membranes may exist for long periods without causing optic neuritis, and the fact that it may result from quite small growths. A slight tissue-irritation may be propagated widely through the brain and pass down the optic nerve, and be the excitant of the neuritis. There is definite inflammation of the sheath when there is adjacent meningitis. The optic papilla seems to be a structure prone to inflammation, as its occurrence from blood-states proves, and when excited, local conditions may augment its intensity. Some other points concerning the relation to its causes will be mentioned in connexion with the maladies in which it occurs (p. 344).

*Atrophy* of the optic nerve, when primary, is revealed by changes in the aspect of the disc. The nerve-fibres waste, and their shrinkage causes the part of the disc they occupy to lessen in bulk. Hence the excavation, instead of beginning at the "cup," begins at the actual edge of the disc, *i.e.* at the opening in the sclerotic, as can be clearly recognised with the ophthalmoscope. The capillaries of the disc lessen and may ultimately disappear. Hence the tint becomes paler and even white. Sometimes the atrophy leaves the colour grey instead of white; this is because the disc was originally full-coloured and the walls of the capillaries persist. Thus the process of atrophy is marked by the slow disappearance of the red tint, rather than by whiteness. The central artery and vein often become smaller, the retina sharing the atrophy, although this is not otherwise to be perceived. The choroid is unchanged, and the edge of the disc therefore remains sharp.

Consecutive atrophy, sometimes spoken of as papillitic or post-neuritic, follows a considerable degree of intra-ocular neuritis. The disc is occupied by new tissue formed during the inflammation, which at first extends beyond the margin, which is then soft-edged. As this undergoes cicatricial contraction the surface becomes white, and the central artery and vein still narrower from compression. Ultimately the tissue subsides to the level of the retina and becomes pure white, but the disc retains its "filled-in" aspect, the margin of the choroid is damaged by the inflammation, and the vessels are more or less con-



cealed as they divide or join at the centre of the disc. These are the characteristic signs of papillitic atrophy.

Secondary atrophy is the result of damage to the optic nerve behind the eye, between it and the chiasma. The appearances resemble those of simple atrophy, but seldom proceed to an extreme degree. Often they are combined with the signs of inflammation, usually slight; it is chiefly met with when the cause is near the globe.

The causes of primary atrophy are defect of vitality on the part of the nerve elements, which may be innate (abiotrophy), or acquired through some toxic influence. The former may occur in several members of the same family, and sometimes seems aided by a blood-state; thus, tobacco in excess may excite it (7). The toxic form is most frequently met with as a sequel to syphilis, although the mechanism of its relation is quite unknown. The active disease either affects the nerve-elements so as to lessen their future vital endurance, or a permanent blood-change is left, which has a similar result. This may be produced many years after the antecedent has ceased to be active, so far as can be judged by symptoms, and the only association may be a degeneration of nerve-elements elsewhere, causing either tabes or general paralysis.

Consecutive atrophy is the result of intra-ocular neuritis. The secondary form is due to the processes that damage the extra-ocular part of the optic nerve or the commissure, retrobulbar neuritis, orbital cellulitis, narrowing of the optic foramen, tumours, especially pituitary, and distension of the third ventricle. Some forms of toxic amblyopia, as from tobacco, present the features of retrobulbar neuritis.

Symptoms.—Primary atrophy entails progressive diminution in vision, involving both acuity and the field, usually from the periphery inwards; they vary in relative amount. Sometimes there is a central loss. Colour vision also fails, usually first for green and red. The failure of sight is only roughly proportioned to the paleness of the disc, the relation depending partly on the original tint. The loss of sight depends on the wasting of the nerve-fibres, which may be disproportioned to the wasting of the vessels. If the colour was but slight, complete pallor may be reached long before vision is lost. If the central loss leads the way, as is usually the case in retrobulbar neuritis and toxic processes, the loss commences by a "periaxial" scotoma, often more or less transversely oval, and always more extensive for colours. Loss of the outer half of each field, "temporal hemianopsia," due to impairment of the decussating fibres from the medial half of each retina, is the effect of damage to the middle of the optic chiasma. Nasal hemianopsia is rare, and due to interruption of the non-decussating fibres on each side of the commissure. Lateral hemianopsia does not come into the symptoms of atrophy. Sector-like defects may result from retrobulbar neuritis. Consecutive (post-neuritic) atrophy causes symptoms which vary according to the degree and character of the damage to the nerve-fibres during the stage of inflammation; often there are very irregular changes in the field, and acuity is always involved. The loss during the neuritis increases during the stage of subsidence, from

the contraction of the cicatricial tissue, but when this is over there is often a slow improvement from the return of some function in the fibres that are damaged but not destroyed.

**The retina** undergoes subacute inflammation in syphilis, and more chronic changes in renal disease, leukaemia, pernicious anaemia, diabetes, and septicaemia, which will be subsequently mentioned. Haemorrhages are common in all these maladies.

**The Choroid.**—The remains of previous choroiditis are more often of medical importance than is the inflammation itself. These are generally small spots of damage, which are white because the sclerotic is exposed, and irregular black accumulations of displaced pigment are seen adjacent to them. They often afford evidence of preceding syphilis, especially of the inherited form. Care must be taken not to mistake for them the choroidal atrophy adjacent to the disc often seen in myopic eyes, or the large amount of pigment sometimes conspicuous between the choroidal vessels, in normal eyes, the *choroïde tigrée* of the French. Another important change is the formation of miliary tubercles in the choroid. They are small, rounded white objects, usually soft-edged, because the margin is concealed and the centre slightly prominent. They are not often seen, but neither are they often looked for, and they occasionally decide a doubtful diagnosis. Nowhere else can tubercles be seen so well during life.

The diseases in which ophthalmoscopic changes occur can be hardly more than enumerated here. More details may be found in the articles on the maladies in which they are especially important.

**Brain.**—Cerebral haemorrhage entails no changes. When neuritis has been found during life, the extravasation has probably been into a soft growth, which then may easily escape detection with the naked eye. But retinal extravasation may coexist with simple haemorrhage. In the case already mentioned in which aneurysms were seen, the patient died a few months later, evidently from a large cerebral haemorrhage. Softening due to embolism occasionally entails slight optic neuritis, apparently from the irritative character of the softening, communicated from the embolus. A similar block in the central artery of the retina may, as it were, demonstrate the nature of the case. Thrombosis in an atheromatous artery only entails effects when the clot is in the internal carotid and retinal branch, but this has seldom been observed during life. When definite neuritis is associated with a focus of softening, the latter will always be found to be due to the breaking down of a morbid growth, unless there is an independent cause for the neuritis, such as Bright's disease.

**Abscess** of the brain causes optic neuritis in about two-thirds of the cases, but rarely so intense as is often seen in tumour. The longer the duration of the abscess, the larger is the proportion of cases with neuritis. Yet it does not seem related to either the seat or the size of the abscess, but it is more frequent and early, the more acute the process of suppuration.

**Tumours** of the brain, to which most cases of neuritis are due, have

been already spoken of. The inflammation has been thought to begin earlier, to reach its height sooner, and to be rather more intense on the side on which the tumour is situated; this is probably true of most cases, but there are exceptions. There is some correspondence between the course of the neuritis and of the growth; a slow, chronic optic neuritis is generally due to a slowly growing tumour. An acute neuritis is usually due to a rapidly growing tumour, but may appear at any period in its course. It is most important to remember that neuritis is only, as it were, a casual consequence of the growth, which may occur early or only begin when the tumour, by its mere size, is about to end the patient's life. Thus, whilst its presence may make the existence of a tumour certain, its absence is of little negative weight, sometimes of none at all. Often a relation may be traced between the amount of headache and the presence of neuritis. As a rule, a compressing meningeal growth has less tendency to cause neuritis than one which invades the brain; I have seen a slow growth from the dura mater which had produced a depression in the parietal lobe into which a large lemon could be placed, without optic neuritis. It is less frequent also in the tumours of the white substance, and is especially common in cerebellar growths.

There seems little relation between the nature of the growth and the occurrence of optic neuritis. It is certainly very frequent with syphilitic growths and with malignant tumours. With tuberculous masses it is often absent, and also with gliomas, even of the hemisphere; still more so with growths springing from the bones or periosteal dura mater. The neuritis is sometimes of prognostic value. The first sign of commencing improvement in a syphilitic or tuberculous tumour may be the diminution of the neuritic swelling. It must be remembered that sight may fail from pressure on the optic commissure in cases of tumour, with or without intra-ocular neuritis, but the temporal hemianopsia is then distinctive.

**Treatment.**—Optic neuritis subsides after an operation for the removal of a tumour that is its cause; even if the tumour cannot be removed, the procedure has the same effect. Sir Victor Horsley was the first to ascertain this and to urge the importance of "decompression" by trephining and opening the dura mater, a procedure which has been lately advocated in Germany and the United States (2).

*Cysts* often cause neuritis because they develop in a morbid growth of which traces only may be visible in the wall. With simple cysts it is rare, but has often been met with as a consequence of hydatids. In no form of cyst does it attain great intensity. *Aneurysms* of large arteries only induce changes if near the optic nerve, when they may cause secondary atrophy, sometimes with visible neuritis from pressure-irritation. Simple internal hydrocephalus causes only secondary atrophy from compression of the chiasma. The presence of optic neuritis is evidence that the ventricular effusion is due to a morbid growth.

*Meningitis* varies in its tendency to cause optic neuritis, according to its seat. When it is over the convexity the effect is late, and often absent, especially in chronic forms. In basal meningitis it is common and early,



often developing before other symptoms make the diagnosis sure. In no form does it usually reach a high degree of intensity, for which there is seldom time in the common form of basal inflammation, tuberculous. There is usually evidence of direct extension to the nerve, and the occurrence of distension of the sheath is distinctly related to the presence of an excess of subarachnoid fluid. The swelling of the optic disc is moderate, and is often paler than in other forms of neuritis; it is rarely attended with haemorrhages. But it becomes sufficient to obscure completely the edges of the disc. Choroidal tubercles are sometimes seen. When the meningitis is septic, the swelling is less pale, and the peculiar white-centred haemorrhages are often seen in the retina; they resemble those found also in the pia-arachnoid, which will be mentioned under "Septicaemia." Epidemic cerebrospinal meningitis rarely causes ophthalmoscopic changes; in very few cases there has been optic neuritis, perhaps coincident.

*Spinal Cord.*—In the rare cases of myelitis in which neuritis has been present, it also seems to be an effect of the cause, and not of the process in the cord. It is curious that it has not been observed in poliomyelitis, or even in polio-encephalitis. No ophthalmoscopic effects of degenerations of the spinal cord are known. The atrophy, so frequent in tabes, and occasionally seen in general paralysis, is a coincident effect of the cause. Insular sclerosis, which is not a purely spinal affection, is often attended by simple primary atrophy of the optic nerves, with its usual effect on vision, but having little tendency to progress beyond a moderate degree. The occurrence of this in a malady which seems to begin by neuroglial overgrowth, is one of the many mysteries of this disease; but it is suggestive, since the neuroglia and nerve-fibres have a common origin. When an islet of sclerosis develops in the optic nerve, secondary atrophy ensues, usually partial, with a sector-like defect in the field of vision. Sometimes slight papillitis precedes atrophy.

*Functional diseases* of the nervous system do not entail ophthalmoscopic changes. An apparent, but perhaps not real, exception is presented by chorea; moderate neuritis may develop in rare cases and pass away as this malady subsides. It is probably a coincident effect of the blood-state; analogous to the associated endocarditis. In idiopathic epilepsy no changes are observed, nor are they present in the organic form, due to an old stationary lesion. The presence of optic neuritis indicates the existence of a tumour, which may cause attacks closely resembling those of idiopathic epilepsy, and these may be the only symptom even during years. So too in cases in which similar attacks are due to a stationary tubercle, there may be evidence of past optic neuritis.

Neuralgia of the fifth nerve has rarely been attended by atrophy of the optic nerve on the side of the pain. The mechanism by which it is produced is not known. Migraine is often preceded by transient disturbance of sight. Very rarely there is permanent impairment of vision in one eye, with the signs of neuro-retinitis, perhaps due to thrombosis.

*Diseases of the Blood.*—Anaemia from haemorrhage is sometimes



followed by loss of sight, the onset being immediate in about a quarter of the cases in which the sudden loss has caused unconsciousness. In others it comes on after a few days, and in rare instances after a fortnight. It is more common after spontaneous than traumatic hæmorrhages, and that from the stomach or bowels, or from the uterus after childbirth, is the most frequent cause. It occasionally follows venesection, hardly ever a surgical operation. The loss of sight may be sudden, or may develop during a few days; sometimes it is preceded by pain behind the eyes. Rarely unilateral, both eyes usually suffer, and the loss is complete and permanent in about half the cases; perfect recovery has occurred only in a fifth; partial in a third, with irregular loss of the fields. Very rarely the ophthalmoscopic appearances have been normal. Usually, in the early stage, there are signs of inflammation, diffuse opacity of the retina and swelling of the papilla; sometimes there are numerous hæmorrhages. The neuritis rapidly increases. The arteries are usually small, but not so small as in embolism. In severe cases the retinal changes subside to a cicatricial state, compressing the vessels, and inducing atrophy of the nerve, the veins also becoming narrow. The precise mechanism by which the ocular affection is produced is still mysterious. Von Graefe explained it by an extravasation in the nerve behind the eye, but of this no trace has been found in the cases examined after death. Various other unproved hypotheses have been framed to account for it, one of which ascribes it to disturbance of the relation of the general and intra-ocular circulation (Ulrich). From the great differences presented by various cases it seems probable that several processes take part in various degree. A sudden derangement of the delicate nutrition of the nerve-elements of the retina may have effects which run an independent course, and are augmented by the imperfect blood, sometimes so as to attain the degree of intense inflammation.

**Chlorosis.**—The pallor of the choroid and of the columns of blood in the vessels may be striking; the veins appear, and probably are, unduly wide from atony and flattening due to the intra-ocular pressure. Hæmorrhages are hardly ever seen in this condition, in which the hæmoglobin is lessened out of proportion to the diminution in the number of the corpuscles. But optic neuritis occurs in rare cases, double, and sometimes reaching such a degree as gravely to impair sight. Its mechanism is not known, but its rapid improvement if iron is given, and the patient kept at rest, seems evidence of its relation to the blood-state. The importance of rest is to economise the defective hæmoglobin and prevent its disproportionate consumption in muscular exertion. (*Vide* also Vol. V. p. 716.)

**Pernicious Anaemia.**—The same pallor of the blood is seen in the fundus as in chlorosis. When the corpuscles fall below 25 per cent hæmorrhages occur in the retina, often numerous, and striated or flame-shaped, from their position in the nerve-fibre layer. Small white spots often accompany them, due to leucocytic cells and products of degeneration

of nerve-elements damaged by the extravasations, which usually soon disappear. Slight neuritis may coexist. Vision is impaired only if a haemorrhage happens to be near the macula lutea. Aneurysmal dilatations of the capillaries are found after death which often results from haemorrhages elsewhere.

Leukaemia is attended with a similar ultimate haemorrhagic tendency, even greater in degree, of which retinal extravasations may be the first indication. The pallor of the choroid and retinal vessels is conspicuous and often attended by a change to an orange tint. The veins become extremely broad and sometimes tortuous, the arteries narrow. The extravasations are scattered over the whole retina, and are usually striated, but sometimes large and rounded, infiltrating all the layers; they have been known even to break through into the vitreous. White spots are also common, rounded or irregular in shape, sometimes with a halo of haemorrhage around them. They are often numerous in the periphery of the retina. They consist chiefly of leucocytes, like those of the blood, and the capillaries are often found distended with them; they are supposed to escape into the retina and give rise to the white spots, but these contain also products of degeneration of the nerve tissue. Papillitis may accompany the retinal change, with leucocytic infiltration and oedema; in some cases it reaches a condition resembling "choked disc," doubtless from the compression of the veins within the papilla. Rarely a leucocytic infiltration of the choroid has been observed. Interference with vision depends on the position of the changes, and their relation to the macula. These alterations have been hitherto observed chiefly in the myeloid form, and occasionally precede a fatal haemorrhage in the brain.

Purpura and Scurvy.—In these maladies, especially in the former, retinal haemorrhages are seen in the more severe degrees of the malady. They resemble those of pernicious anaemia, but are of less grave significance.

Septicaemia and infective endocarditis are often attended by retinal haemorrhages, which are peculiar in aspect and sometimes of diagnostic importance. They are more or less rounded, often striated at the margin and surround a smaller white spot. In apparent size they vary from a quarter to half a disc-diameter, and are scattered over the retina, near or away from visible vessels. Obstruction of capillaries by minute organisms is doubtless their cause, but these are seldom found because they are concealed by the results of the inflammation they quickly cause. Quite similar haemorrhages may be seen in the membranes of the brain in such cases. I have seen them in infective endocarditis following chorea, but they are also met with apart from any affection of the heart, and are especially common in puerperal septicaemia. They may decide the diagnosis, as in one case under my observation, which was thought to be enteric fever. They have always a grave prognostic significance, but do not preclude recovery. When septic meningitis exists, optic neuritis is common from extension, but rarely has time to reach a considerable degree.

Behind the eye intense inflammation may be found in the nerve. A rare condition of the retina in septicaemia presents many minute white spots with few haemorrhages, the flecks being most numerous near the papilla and around the macula. It has been termed "Retinitis septica."

*Diabetes*, of considerable degree and duration, is sometimes attended by retinal changes. More frequently impairment of sight is due to cataract; rarely to atrophy of the optic nerves, or to retrobulbar neuritis, analogous to the inflammation of nerves met with elsewhere. The latter causes a central scotoma, larger for colours than for white, peripheral vision being normal. The change in the nerve is in the axis at the back of the orbit. The retinal change in diabetes is bilateral and consists of small whitish spots and sometimes areas of larger size and irregular shape and outline. The small flecks have less tendency to a circular arrangement about the macula than is seen in albuminuria. These may exist alone, but haemorrhages are often present, sometimes large and attended with signs of adjacent parenchymatous changes. Occasionally there is a definite degree of papillitis. The haemorrhages are no doubt due to aneurysmal dilatation of the capillaries, which are commonly found after death, not only in the retina but in the choroid. Extravasations in the latter may project into the retina and even the vitreous, giving rise to permanent opacities, the coexistence of which is a characteristic of this condition. The dependence of the changes on the malady is shewn by their disappearance when the sugar is lessened by dietetic treatment, and by their return with an increase in the glycosuria.

*Bright's Disease.*—Of all extra-cranial maladies, renal disease most commonly causes ophthalmoscopic changes. In most cases of chronic disease of the kidneys, especially the contracted form, the arteries are small, in correspondence with the tension of the pulse which is ascribed to the arteriolar contraction, here alone visible. The walls of the arteries become thickened in the same cases; the central reflexion from the column of blood is unduly bright, and the white line on each side becomes more conspicuous and extensive. Where an artery crosses a vein, the compression of the latter is greater than is ever seen in health. The thickening sometimes depends on a hyaline degeneration which invades all the coats. Rarely the change is sufficient to render the column of blood invisible at certain regions. It may even cause obliteration of the cavity of the vessel. Very rarely distinct aneurysmal dilatations are seen on the larger arteries. The veins are less frequently changed, but are distended beyond the spot at which a thickened artery crosses them, and they sometimes present varicosities. In the capillaries, dilatations are commonly found after death. With such changes in the vessels, it is not surprising that haemorrhages are almost constant when the retina suffers. They are especially striated, or lanceolate and pointed, from their occurrence in the nerve-fibre layer, but may be more or less rounded when they occur in the deeper layers, where they may be large, and may even detach the retina from the choroid or burst into



the vitreous. A single extravasation often exists without other alterations in the retina, but, when multiple, they are associated with white spots or areas, and these may exist alone. They are the most characteristic feature of "albuminuric retinitis." Sometimes they are only small spots or flecks, scattered over the posterior half of the retina, and often arranged in an irregular stellate figure around the macula. These small flecks are the chief feature in the "degenerative" form, met with especially in the later stage of granular kidney. Around the optic disc they are often larger, and are accompanied by the small striated haemorrhages. The white spots are chiefly due to local degeneration of the nerve-fibres; they first present varicosities, and then rounded bodies form, containing granules or globules of fat. The fibres of Müller undergo similar changes, and it is to the arrangement of these around the macula that the stellate disposition of the flakes is due. Near the larger spots, areas of slighter opacity may often be seen, due to the separation of the elements of the retina by a coagulable fluid, which sometimes occupies considerable spaces. The optic disc is often normal in this form, but sometimes presents slight swelling and obscuration. Occasionally a more definite degree of papillitis, out of all proportion to the affection of the retina, is met with. It may be such as to resemble the slighter neuritis from cerebral tumour, and is sometimes mistaken for such when the retinal changes are so slight as to be overlooked, and headache is prominent.

The acute form occurs in acute nephritis, and sometimes supervenes on the chronic form. In this the white areas are much larger, and may be a disc-diameter or more in width. They are more or less rounded, and are soft-edged. Their cause is the rapid degeneration of the tissue-elements throughout large areas, and the tissue-change seems to excite an extensive infiltration with leucocytic cells. There may be also a wider oedematous swelling of the retina which may extend to the disc and there become more intense. Numerous haemorrhages occur adjacent to these white spots, mostly striated, but sometimes large. In cases which improve, the white patches shrink, and the haemorrhages disappear as the blood becomes absorbed; often some evidence of residual damage can be seen resembling the degenerative form, but it is remarkable how little trace may ultimately be left of an acute albuminuric retinitis. This acute condition occurs, not only in acute nephritis, but sometimes in the albuminuria of pregnancy. When it supervenes on the chronic form, whether primarily such or the result of a preceding attack of acute Bright's disease, it is generally a terminal sign. Its recognition is thus of great importance. But in acute nephritis it is often survived, and sometimes in chronic disease if treatment is effective.

When haemorrhages are abundant, the condition has been described rather needlessly as an "haemorrhagic" form, and that in which neuritis preponderates, as a "neuritic" form, a variety which has more justification. When there is considerable swelling, compression of the veins may take place within the papilla, and their distension beyond may be almost like "choked disc." This form has seemed to me most frequent



in cases of renal disease with much headache, by which the semblance of a cerebral tumour is made more striking, and the danger of error increased. Indeed, post-neuritic atrophy may be left if the patient survive.

Choroidal changes are rare. The most common is an extravasation which leaves a spot of atrophy. Detachment of the retina is a rare occurrence. Haemorrhage into the vitreous sometimes occurs by the escape of blood from a large extravasation; the patient may be unaware of the accident until he accidentally finds himself blind in one eye.

Albuminuric retinitis causes slighter symptoms than the retinal changes might suggest. In general, the macular region itself is spared, and the peri-macular changes occur in separate points and cause no considerable impairment of central vision. The loss produced in the field of vision by the larger areas of disease is unnoticed by the patient, because, though the retinitis is always bilateral, the lesions in the two eyes do not correspond in their effect. Vision is often temporarily lost from uraemic amaurosis, without relation to the retinal affection.

*Tuberculosis* may be manifested by tubercles in the choroid, already mentioned. One was visible in a girl with obscure chronic peritonitis, and made a doubtful diagnosis certain. Only through meningitis, and diseases of the cranial bones, and growths of the brain, does tuberculosis indirectly cause ophthalmoscopic changes. The occurrence of an intra-ocular tuberculous growth is very rare, and so are other tumours within the eyeball, which may be left to ophthalmic science.

*Syphilis*.—Acute syphilitic neuro-retinitis is scarcely within the province of this article. The inherited disease may present the same manifestation of the constitutional malady, and of the post-syphilitic degeneration, in the eye, as we see when it has been acquired. Especially important are the indications of previous choroiditis in the spots of pigmented atrophy, which are enduring. Optic-nerve atrophy is usually associated with the symptoms of tabes, and has the same progressive tendency as in adults.

*Gout*.—The influence of gout in producing renal disease often leads to albuminuric retinitis. Haemorrhagic retinitis, with small striated or flame-shaped extravasations scattered over the entire fundus, has been met with, usually in one eye only, in young persons with strong gouty inheritance. It has been ascribed to partial closure of the central vein behind the eye by thrombosis on the wall; there is not the distension of the retinal veins which results from complete thrombosis. In older subjects localised haemorrhage may result from compression of a vein by a thickened artery. Another affection, met with at any age, and often in the first half of adult life, which is associated with inherited gout, is retrobulbar neuritis. It seems similar to the inflammation of nerves that is met with elsewhere. According to the proximity of the globe, slight signs may be visible in the eye; when the damage is great, the disc presents, after a time, "secondary atrophy." Irregular changes in the field are produced according to the fibres chiefly affected, but a central

loss is especially common. It usually begins in one eye, and may be limited to it, but often the other eye suffers also, either from the first, from symmetrical neuritis, or else later, and then perhaps from migration by the optic chiasma. The characteristic loss from chiasmal damage seldom occurs in these cases, but there are others in which the inflammation seems to begin in the commissure, since temporal hemianopsia is present, often irregular. It is not progressive, and other symptoms of intracranial disease are wanting. But in the absence of post-mortem evidence the assumed nature of these cases is unproved.

*Lead Poisoning.*—Besides the transient amblyopia, apparently due to the direct action of the poison on the nerve-centres, progressive optic-nerve atrophy is met with in rare cases. In the cerebral disturbance which may attend the rapid action of lead, “encephalopathia saturnina” (and sometimes without it), optic neuritis often occurs, with considerable swelling and haemorrhages. It may pass away, but when the inflammation is prolonged, consecutive atrophy is left, with enduring impairment of sight. Care must be taken not to mistake for this the neuritis that may result from kidney disease, which may be induced by secondary saturnine gout.

*Alcohol.*—Chronic alcoholism is said to cause amblyopia, especially impairment of central colour-vision, and sometimes a slow moderate degree of atrophy. Congestion of the disc has been described in some cases, especially when chronic thickening of the meninges is produced. A source of uncertainty exists in the fact that most sufferers from amblyopia have been also smokers. In acute alcoholic poisoning, congestion of the disc has also been described, and a diffuse retinitis has been very rarely observed. But it is remarkable how rare it is to meet with ophthalmoscopic changes in cases of alcoholic multiple neuritis.

*Tobacco.*—Amblyopia from this cause is of chief medical importance in its liability to cause error in diagnosis. Its characters are the central dimness of sight, greater for colours than for white light, probably due to a primary affection of the macular fibres and a secondary inflammation of the retrobulbar fibrous tissue in the nerve. Indications of this may be visible in the disc, as a slight degree of inflammation.

*Acute Specific Diseases.*—After enteric fever, measles, influenza, and especially after scarlet fever, optic neuritis has been occasionally observed. It seems to be a direct effect of the toxic state of the blood, for it has occurred with cases of scarlet fever in which there was no renal complication, and the occurrence of myelitis after measles is well established. The neuritis may be so considerable as to impair vision in grave degree, and to leave behind it consecutive atrophy.

*Malaria* has been known to give rise to retinal haemorrhages, which are generally striated, and leave behind them punctiform opacities in the retina, and sometimes large white spots. Occasionally small white spots have occupied the centre of extravasations, as they do in septicaemia. Their precise mechanism is uncertain. Very rarely neuro-retinitis has been observed, and deposits of pigment have been seen beside the retinal vessels.

**Optic Abiotrophy**, wasting of the nerve-elements from defect of vital endurance, seems to underlie the form of atrophy which affects several members of a family, even in more than one generation. Isolated cases are sometimes met with which seem to be of the same nature. An important point is the frequency with which some adventitious influence appears to excite the onset. In the family cases, in which its essential nature cannot be doubted, the onset has often followed an acute specific disease, or has apparently been excited by tobacco. This sequence of events illustrates the ease with which what is only an excitant of disease may be regarded as the sole element in its causation.

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## DISEASES OF THE NERVES

DISEASES OF THE SPINAL NERVES.

DISEASES OF THE CAUDA EQUINA.

MULTIPLE SYMMETRICAL PERIPHERAL  
NEURITIS.

HERPES ZOSTER.

DISEASES OF THE SYMPATHETIC  
SYSTEM.

DISEASES OF THE CRANIAL  
NERVES.

TRIGEMINAL NEURALGIA.



## DISEASES OF THE SPINAL NERVES

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Revised by R. A. FLEMING, M.D., F.R.C.P.Ed.

**SENSATION.**—Our knowledge of the forms of sensation and of the nerve-paths of sensory impulses has been placed on an entirely new basis by the researches of Drs. Head, Rivers, and Mr. Sherrington. The earlier impressions of Max von Frey and Prof. Sherrington undoubtedly led up to this important addition to our knowledge. Neurology is the richer from the self-sacrifice of Dr. Head, whose left radial and external cutaneous nerves were divided at his request in April 1903. With Dr. Rivers and Mr. Sherrington he then studied the resulting sensory changes, no motor nerve-fibres being affected by the operation. Prof. Sherrington had previously demonstrated the existence of sensory fibres in muscular nerves. The conclusions of Dr. Head and his colleagues may be summarised as follows: (1) *Deep Sensibility*—Fibres capable of conducting sense-impressions and pain-sensations on the application of excessive pressure run with the branches of the nerves to the muscles, tendons, and joints. The knowledge of movements of joints, muscles, and tendons and of the position of a limb is gained by means of these fibres, but they are not influenced by dragging of hairs or mere pinching of the skin. After the division of all sensory fibres to the skin, the denervated part remained sensitive to pressure, which, if extreme, caused pain. Moreover, the spot stimulated could be localised, and the position of the fingers and the movement at the joints could be accurately appreciated. But such an area was entirely insensitive to stimulation of the skin with cotton-wool; stroking or pulling the hairs produced no sensation either of touch or pain, and the two points of the compasses could not be distinguished until they were separated to a distance greatly in excess of that required on the normal skin. (2) *Cutaneous Sensibility*—The manner in which sensation is restored after division of sensory nerves to the skin led these observers to the conclusion that it is due to two systems of sensory nerves. (A) *Protopathic*. The fibres which subserve these sensations convey painful cutaneous stimuli and the extremes of heat ( $45^{\circ}$  C. and over) and cold ( $26^{\circ}$  C. and under). The protopathic fibres of adjacent nerve-trunks overlap greatly in their areas of supply, especially on the upper extremity. (B)

*Epicritic.* The fibres and end-organs of this system enable us to appreciate light touch, lesser degrees of temperature, especially  $26^{\circ}$  to  $40^{\circ}$  C., and the discrimination of two points in the compass test. There is practically no overlapping of adjacent epicritic areas as far as the main nerve-trunks, such as the median and ulnar, are concerned. Protopathic and epicritic domains not merely differ as regards overlapping, but the two forms of sensibility are restored at different times after union of a divided nerve; this was clearly demonstrated during the course of Dr. Head's experimental nerve-section, because protopathic sensibility returned long before the epicritic, and could therefore be separately investigated. These discoveries and other results obtained in the course of this research necessitate a revision of our methods of examining sensation.

Tactile localisation is possible by deep sensibility alone if sufficiently forcible pressure be applied, and the position of limbs and movements of joints can be recognised by means of impulses carried along the same deep fibres. Protopathic localisation is less exact. The protopathic fibres recover their function after division before the epicritic, and it is found that stimuli are apt to be widely diffused and often referred to parts distant from the point touched. If pressure is eliminated, it is impossible to localise the exact spot touched by protopathic sense alone. Epicritic localisation, on the other hand, is absolutely exact.

Blix in 1884 described heat and cold spots, the cold spots being from two to four times as numerous as the heat, and there are pain spots which are much more numerous than the cold. The heat spots being comparatively few are easily studied. The cold spots being closer together are more difficult to determine, and the pain spots, which are still closer, are correspondingly more difficult. These heat, cold, and pain spots regain their functions long before epicritic sensations are fully restored; the explanation of this recovery is that heat, cold, and pain spots depend on protopathic nerve-fibres for the conduction of their stimuli.

Touch spots, on the other hand, are epicritic. Over hairy regions they are closely related to the roots of the hairs, and any movement of the hair sets up tactile impressions. Protopathic sense-organs have a high threshold. The heat spots do not react to a temperature below  $37^{\circ}$  C., the cold spots to a temperature above  $26^{\circ}$  C., and the pain spots require a pressure of 26 grams. Epicritic sense-organs have a low threshold; they respond to temperatures between  $26^{\circ}$  C. and  $38^{\circ}$  C., and they have a much more sensitive pressure-recognition; for example, the back of the hand requires 12 grams. The glans penis was found to be endowed with protopathic and with deep sensibility, but not with epicritic sensibility, and the comparison of experiments conducted on it and on the area of skin on Dr. Head's hand, which had recovered protopathic but not epicritic sensibility, was of great value.

**Methods of Examination.**—Before considering any nerve lesion it is well to describe briefly the method of examining the limb in a case of



nerve injury. In addition to the exclusive supply of an area of skin by any one of the larger nerve-trunks, there is a larger area to which the nerve supplies fibres in common with neighbouring nerves. The intermediate zone is the area between the outline of loss of sensibility to prick and the loss of sensibility to light touch. The extent of loss of epicritic sensibility usually is greater than that of protopathic.

The first thing which the physician should do is to determine any area of hyperaesthesia which may be present, and then to test sensibility to light touch by means of a brush or cotton-wool, and sensibility to prick by drawing a sharp needle across the skin from the normal towards the anaesthetic parts. Considerable differences in the results obtained may be due to causes which have nothing to do with the extent of the nerve lesion. Any undue fatigue of the patient, any difference of temperature of the day, and even the condition of the patient's health, may all affect the accuracy of the examination. The patient's eyes should be bandaged, and care taken not to tire him by needless repetition, and ample time should be allowed, so as to render the results as free from error as possible. Epicritic sensation should be tested by the use of the compasses, the legs of the compasses being separated to a known distance, and the patient should be touched sometimes with one leg, sometimes with both, and asked whether he recognises the application of two points or one. A horny hand may, under ordinary conditions be absolutely insensitive to cotton-wool or the application of the brush, and as the skin tends to desquamate over the affected area lightly applied stimuli may not be appreciated. The presence of hairs also introduces a possible error when protopathic sensibility is retained. The application of test-tubes containing water at different temperatures is of value, although the appreciation of temperatures between 25° and 40° C. may be too elaborate for ordinary examination purposes, and the use of warm water and of ice or cold water is sufficient in most cases. Cattell's algometer may be used for testing the pain of the deep sensibility fibres. I have found Rivers' modification of Cattell's instrument easy to work. In some cases it may be desirable to investigate the patient's capability of recognising the position of joints and of passive movements of muscles.

It is most important to determine if the nerve distal to the lesion retains any faradic irritability, and if the muscle or muscles supplied by it shew a complete or partial reaction of degeneration (see Vol. I. p. 456). The prognostic value of the partial as compared with the complete reaction when the galvanic current is applied to the muscle cannot be overstated, for complete absence of galvanic irritability in the muscle or muscles makes it highly improbable that any surgical operation will restore the functions of the nerve. We have therefore to investigate the epicritic, protopathic, and deep sensibility sensations, and also the electrical reactions of nerves and muscles. Further, we should note any obvious atrophy of the affected muscles.

The appearance of the skin, quite apart from definite blebs or sores,

may be very striking. In complete division of the nerve the skin of the affected area retains its epithelium, which forms a rough dry layer; there is absence of sweating of the affected part, and slight injuries, such as those made by the needle in the course of testing sensation, may remain apparent for several days. When protopathic sensation is in abeyance the skin is very liable to suffer from any slight irritant; for example, a burn may be produced by water which could not possibly injure a healthy skin, and it is probable that in this way not a few of the trophic sores and blisters originate.

When the lesion is incomplete there may not be any permanent motor or sensory changes whatsoever. In some nerves a considerable number of the axis-cylinders can be divided without producing any symptoms or signs. In other nerves, for example the sciatic, which divide far above the point where important branches pass off, a partial injury of the nerve may more or less completely divide one of those branches. Mr. Sherren has shewn the fallacy of the oft-repeated statement that in incomplete injuries of nerves the motor fibres suffer more than the sensory fibres. He finds that one of the first evidences of an incomplete division of a mixed nerve is a change in epicritic sensibility, as may be well shewn by either the cotton-wool or compass test. Not infrequently the muscles, although paralysed, still react to the faradic current. Pain is one of the most prominent symptoms, and is specially severe in gunshot wounds; it may be of an intense burning character, and the irritation may be followed by an ascending neuritis. As a rule, the skin of the affected fingers does not become glossy, but is apt to be rather red or mottled and may be free from hairs. There is generally profuse sweating in place of the absence of sweat which is so characteristic of complete division, and it is stated that the nails of the affected fingers may grow faster than normal. Sometimes bullae, and occasionally ulcers, appear, but these trophic changes depend much on the degree of irritation present. There is as a rule no difficulty in diagnosing between a complete and incomplete division of a nerve, but sometimes it is desirable to allow a week or two to elapse before giving a definite opinion.

**CLASSIFICATION.**—The consideration of the diseases of the spinal nerves will be facilitated by a division into two groups: one, of a more general character, will contain the pathological and clinical features common to the different forms of disease; the other, of a more special character, the several forms themselves.

#### GROUP I.—GENERAL FEATURES

The subjects which fall under this head are neuritis, tumours, pressure, and wounds.

**NEURITIS.**—**Local Neuritis.**—There are obviously two distinct forms of neuritis which depend on the nature of the causal agent and also on the site of the inflammation: (1) *Interstitial neuritis* implies that the

connective tissue in one or other of three positions is specially affected. It may be (a) the epineurium or the connective tissues surrounding the funiculi of the nerve-trunk; (b) the perineurium or the connective tissue forming the sheath of each individual funiculus; or (c) be limited to the delicate connective tissue inside the funiculus which forms the septa running across the funiculi and dividing the bundles of nerve-fibres from each other. The term interstitial neuritis certainly includes inflammation in all these three positions, although it has been suggested that the site of inflammation might be indicated by the use of the words epineuritis, perineuritis, and endoneuritis. Not infrequently, however, in interstitial neuritis the inflammation is not limited to one of these alone, but may involve them all. (2) *Parenchymatous Neuritis*. In this form the nerve-fibres themselves are affected. It is often the result of a toxic agent, and very commonly an interstitial neuritis in the funiculi is associated with implication of the nerve-fibres. In a given case of neuritis it may be difficult to decide whether the morbid change is degenerative or inflammatory.

*Etiology*.—Rheumatism, gout, and exposure to “cold” may induce a localised perineuritis, much in the same way as other connective tissues become inflamed in these conditions; but it is quite possible that the active agents in rheumatism and gout may in some cases attack the nerve-fibres themselves, causing a true parenchymatous neuritis. Cold probably always causes interstitial inflammation, by means perhaps of a paralytic hyperaemia.

A nerve may also be injured by wounds, bruises, muscular strains, fractures or dislocations of bones, tumours, abscesses, bed-sores, or any contiguous focus of inflammation. Obviously in all these cases perineuritis is first produced, although in time the funiculi may be involved, and eventually the nerve-fibres themselves. There are many well-known instances of such local neuritis. Not infrequently a suppurating joint, or even an acute non-suppurating synovitis, may induce a local neuritis in neighbouring nerves; sometimes in syphilitic and other inflammations of the membranes of the brain and cord, a localised neuritis may be set up in the cranial or spinal nerves which arise at the site of the lesion. After a fracture neighbouring nerves may be damaged by the callus thrown out.

Lastly, there are certain states of the blood in which a limited neuritis may be determined by some local cause. Probably, as above stated, rheumatism and gout can act in this way; certainly in acute tuberculosis with much toxic absorption, in alcoholism, and as the result of any of the toxic causes which generally give rise to a multiple neuritis, the lesion may be confined to one nerve. Diphtheria is perhaps the most striking illustration of such limitation of a truly toxic agent in its sphere of attack; although in some cases a more general invasion of many peripheral nerves may ensue. Syphilis, cancer, and leukaemia may bring about a toxic neuritis; either through the blood or by direct infiltration of the nerve tissue with specific cells, causing local inflammatory changes.



*Morbid Anatomy.*—In interstitial neuritis there is exudation into the connective tissue; and, dependent on the nature of the inflammatory process, there may be complete absorption, organisation of inflammatory lymph, or in infective cases even suppuration. The effect on the nerve-fibres depends on the amount of pressure exercised and the nature of the exciting cause. The affected part of the nerve is reddened and swollen; the exudation infiltrating the sheath is sero-fibrinous or jelly-like, containing a varying number of cells, especially around the vessels, often in well-marked groups, and not infrequently capillary haemorrhages.

Microscopically these changes are best studied where the funiculi are affected. Here the exudation is very distinct, especially just within the sheath of the funiculus and along the lines of the septa; it is always most marked near the vessels, and leucocytes may be seen in the effused

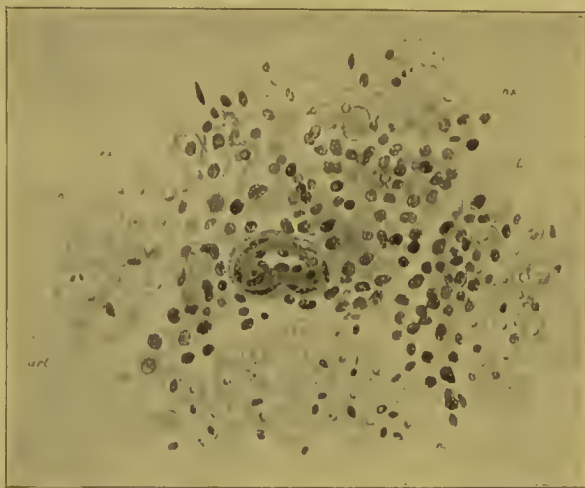


FIG. 62.—Right sciatic nerve from a case of alcoholic neuritis, shewing recent leucocytic exudation around arteriole. *art.* Arteriole; *ex.* exudation; *l.* leucocytes; *n.* normal nerve-fibres; *nz.* degenerated nerve-fibre.

lymph, especially around the vessels. As the sheath of a funiculus is proportionally strong and inelastic, any great amount of effusion implies serious pressure directly on the nerve-fibres, which must inevitably suffer.

*Parenchymatous neuritis* implies the involvement of the nerve-fibres themselves. The axis-cylinders, the myelin sheaths, and the neurilemmal sheath all participate; and as the lesion is one implicating the whole neuron, the nerve-cells from which the axis-cylinder processes arise shew chromatolysis, eccentric position of nuclei, etc. In the nerve the axis-cylinders break up, there is segmentation of the myelin sheath and proliferation of the neurilemmal nuclei. I have endeavoured elsewhere (6) to shew that the parenchymatous changes in the nerve are associated with exudations of inflammatory lymph, leucocytes, or blood which occur in the neighbourhood of the vessels in the funiculi, and that the small arteries shew great hyaline swelling of the media, with proliferation of nuclei in the intima, media, and adventitia. The severity of these



exudations may explain why, although parenchymatous neuritis is, as a rule, greater in degree, the further the nerve is traced towards the periphery, it often happens that less intensely affected sections of nerve are succeeded peripherally by parts less affected. The greater the severity of the neuritis, the more marked are the exudations and vascular changes. The changes in the affected muscles do not call for any special description.

*Signs and Symptoms.*—The symptoms of local neuritis vary with the extent and position of the inflammation and the particular nerve concerned. There may be high temperature, malaise, and considerable



FIG. 62.—From the left sciatic nerve of a case of alcoholic neuritis shewing exudation, with commencing organisation, and the changes in the coats of the arteriole. *art.* Arteriole; *ex.* exudation; *fn.* newly formed connective-tissue fibres; *e.n.* endothelial nuclei; *me.* media; *ad.* adventitia; *ad.n.* nuclei of adventitia.

constitutional disturbance, which disappear in a few days; in milder cases these phenomena may be absent. The chief sensory phenomenon is pain felt in the nerve, often radiating towards its radicles, or diffused over the whole limb. The pain is burning, gnawing, or boring, and is increased by digital pressure over the affected nerve, or by movement if thereby the contracting muscles put any strain on the nerve. The pain is often worse at night, and is increased by exercise, as well as by dependent posture, or anything causing passive congestion of the limb. The skin is often extremely hyperaesthetic, and there may be local redness or oedema. When the inflammatory condition has interrupted the conduction of nerve impulses, local anaesthesia not infrequently appears; sometimes there is perverted sensation; and in some rare and inexplicable cases there are similar, though slighter, changes in the

corresponding part of the opposite limb. Palpation when possible may demonstrate a distinct increase in the size of the affected nerve.

Where there are many motor fibres in the nerve concerned there is paralysis with wasting of muscle, in degree depending largely on the amount of interference with function. The muscles may simply be weakened, or they may become absolutely paralysed, and give a well-marked reaction of degeneration. The muscles are often tender, extremely painful on attempted movement, and not infrequently shew fibrillar twitchings.

The *trophic changes* are described on p. 112 *et seq.*

*Diagnosis.*—In the majority of cases of local neuritis the diagnosis presents little difficulty. Definite sensory and motor phenomena referable to one nerve, localised pain elicited on pressure along the line of the nerve, and the recognition of an etiological factor in the case, simplify the diagnosis. It must be remembered that the pain of neuritis is of much longer standing and more continuous than neuralgia, although the pain of localised neuritis might with justice be called neuralgia. Many neuralgias have local oedema and distinctly painful spots, which correspond to nerve-trunks or their branches; but a marked alteration in sensation, especially anaesthesia, and paralysis with muscular wasting are absolute proofs of neuritis. Rheumatism and gout may cause neuritis, but pain produced by either of these agents is more likely to be due to inflammation about tendons or joints.

*Prognosis.*—The prognosis depends largely on the nature of the individual case. Acute neuritis may disappear in a few weeks if the cause can be successfully and promptly removed. Perineuritis and interstitial neuritis must of necessity be tedious, because inflammatory lymph has been effused, and absorption must occur before cure can be effected. Rapid improvement under treatment always renders complete recovery more probable; whilst persistent inflammation, however slight, will almost certainly be very protracted, and the cure may be incomplete. Rheumatism and gout often cause neuritis lasting months instead of weeks; partly because of the difficulty of eliminating the toxic agent, and partly because inflammatory lymph, if not removed, organises: connective tissue is thereafter extremely apt, by contraction, seriously or even permanently to compress the nerve-fibres in the affected funiculi. In such cases the axis-cylinders may not be interrupted, but the myelin sheaths are thinner than normal, and certainly clinical experience teaches that conduction of impulses is greatly hindered by such a condition. The best prognosis must therefore be assigned to neuritis which is the result of an injury. A less favourable prognosis should be accorded to toxic cases, in which the toxin cannot be removed at once; a still more grave prognosis must be assigned to all chronic cases with a duration of months or years.

*Treatment.*—The cause must be searched for and removed. Any injury must be suitably dealt with, the utmost care being taken to prevent a nerve, exposed in a wound, from becoming septic. Rheumatism, gout,

and syphilis must be met by specific management; it is a good routine practice to give salicylate of sodium, or salol, where, with no certain rheumatic history, there is even a faint probability of its existence.

In acute cases it is always useful to act on the bowels by one or more doses of a saline hydragogue cathartic, or blue pill followed by a purge; to aid elimination by the kidneys with diuretics; and lastly, to increase diaphoresis by baths, especially Turkish and vapour baths. Rest, removal of inflammatory products by absorption, and suitable means for keeping up the nutrition of muscles, must be specially referred to. Rest can be most satisfactorily secured by confining the patient to bed, or at least keeping the affected limb absolutely quiet. A splint, well-protected by wadding, will be found useful for this purpose, and every care should be taken to impress the patient with the necessity for this procedure. Sedative applications are of great value for the relief of pain. Continuous bathing of the affected part with hot water; hot fomentations, with or without the addition of tincture of opium; poulticing the limb; and the use of liniments, such as the British Pharmacopoeial belladonna, aconite, and chloroform liniments, are most soothing. Leeching is likely to be of value when the local inflammation is recent and severe. Where the pain is harassing, or unbearable, local hypodermic injections of morphine or cocaine are often beneficial; but they should only be employed along with absolute rest to the affected part, as any use of the limb rendered possible by a hypodermic injection of morphine is certain to be harmful. Obviously counter-irritation and sedative applications are of most use in the acute cases.

But in every form of neuritis at present under consideration there is effusion of inflammatory lymph, and the absorption of this is greatly facilitated by vigorous counter-irritation. Small fly-blisters, or blistering fluid painted along the line of the nerve, or even the application of stimulating liniments, such as *linimentum terebinthinae aceticum*, should be used, provided there be no trophic change in the skin where they are to be applied. Any change in sensation, especially anaesthesia, or any evidence of incipient "glossy skin," should absolutely contra-indicate all vigorous counter-irritation, and should prevent attendants from applying very hot fomentations or poultices. The constant current is recommended, both for the relief of pain and for the removal of exudation; a mild current and the positive pole applied locally should always be used, care being taken to avoid causing muscular contraction by interrupting the current. Potassium iodide is often given, sometimes with marked success; and small doses of mercury and antimony are frequently of great service.

The nutrition of muscles supplied by the affected nerve will require attention; but the faradic or interrupted galvanic currents should never be resorted to for exercising muscles, so long as any acute or subacute inflammatory condition remains. After subsidence of inflammation the interrupted current is of great benefit; but before this occurs it is better either to disregard the muscles, or to try the most gentle of passive movements.

I have found a combination of galvanism and faradism of great



value in cases of neuritis and in all nerve lesions in which it is necessary to maintain the nutrition of the muscles. If a moderately strong faradic current is applied to a muscle and while it is running a weak galvanic current is superadded, the muscular contractions due to the faradic current become much stronger. The point of most practical interest is not so much that the one current intensifies the action of the other, as that the benefit the patient obtains from the faradic current is enormously enhanced by the addition of the galvanic. In a long list of cases rapid improvement followed the use of the two currents simultaneously after the use of one current alone had yielded disappointing results.

Cataphoresis or electric osmosis, by which is meant the giving of electrolytic drugs as ions, has been recently recommended for the treatment of nerve inflammations and pain. This is effected by means of the galvanic current, which converts such drugs into cations and anions; the cations enter the body by the positive pole by which they are repelled, the anions by the negative pole. In this way certain drugs can be made to enter the tissues locally. All metals and alkaloids are cations and should be applied by means of the positive pole to the patient, whilst salicylic acid is an anion and is applied by means of the negative pole. The current should be gradually turned on till 25 or 30 milliamperes are passing. It should be kept up for some time and then gradually reduced to zero before being switched off. Very successful results have been reported by Dr. Dawson Turner and others.

In chronic cases of neuritis, in which some organisation of inflammatory lymph has occurred, friction along the line of the nerve, and energetic and long-continued massage, are often followed by progressive improvement in both sensation and in motor power.

**Neuritis Ascendens.**—In 1861 Remak described a case of ascending neuritis due to an infected wound, the inflammation spreading upwards from a comparatively trivial injury. After a considerable amount of suppuration the wound healed in fourteen days, but three months afterwards the patient suffered from cramps and severe pains, specially in the ulnar nerve, which was palpable as a swollen cord near the internal condyle. It was an undoubted case of infective neuritis. Within a few years many further cases were published, and amongst these a considerable number of instances of so-called ascending neuritis due really to joint affections, to which cause the pains in the line of the nerves and the muscular atrophy were secondary. Feinberg and Lewisohn recorded a number of cases of ascending neuritis. Feinberg, by cauterising the sciatic nerve of a cat, produced paralysis of the hind limbs, incontinence of urine, convulsions, and death. At the necropsy, myelitis was found, and Feinberg called the condition reflex paralysis. Roessingh, Rosenbach, Treub, and Kast repeated Feinberg's experiments, and found that myelitis did not occur unless the wounds were allowed to become infected, and that the ascending neuritis was really an upward extension of a septic, or at least an inflammatory, process along the line of the nerves, and was in no sense a reflex paralysis. Neuritis migrans, which had a somewhat slender pathological basis,



received a severe shock from these results. Neuritis migrans, as the name implies, was supposed to be a form of neuritis which moved in a mysterious way from one portion of a nerve to another, and the hypothesis of a possible reflex paralysis was linked closely with this mysterious migrating type of neuritis. Such a death-blow did the old conceptions of ascending neuritis receive that the condition has only recently regained proper notice. Möbius (1907) does not recognise true ascending neuritis. Oppenheim (1905) considers that it is possible but unlikely, and Bernhardt (1902) does not mention it at all. More recently several papers have appeared (Claude and Lejonne, Bolten and others) which appear to gauge correctly the place of ascending neuritis in diseases of the peripheral nerves. The ordinary form is certainly an ascending inflammatory process, starting at the seat of injury and advancing more or less rapidly along the line of the nerve, and causing such intense pain as to necessitate nerve section or even amputation. Weir Mitchell has recorded a number of these cases, many of them associated with gunshot wounds or sword-cuts on the field of battle. In one case of a different kind a girl transfixed her median nerve with the thin spout of a watering-can. The pain, which extended up the nerve, became so excessive that after excision of bits of the nerve, which afforded temporary relief only, amputation of the arm had to be performed. It seems probable that the lymph-stream is the channel by which the organisms or their toxins proceed upwards. It is a little difficult to exclude a form of what may in reality be ascending neuritis, although it is different in nature to that just described. In an injury to a nerve the scar or process of healing, or possibly the formation of a neuroma, may keep that nerve in a hyperaesthetic state. These cases are generally completely relieved by opening the wound and removing the focus of irritation.

The *clinical features* of ascending neuritis are motor, sensory, trophic, secretory, and vasomotor. The motor are only present in cases in which the axis-cylinders going to muscles have become affected, leading to atrophy and paralysis. Contractures are seldom present. The sensory changes include paraesthesia, hyperaesthesia, and anaesthesia. When the neuritis is interstitial there are some signs of irritation, when it is parenchymatous there are some definite paralytic results. The most typical sensory change is unquestionably a form of paraesthesia, consisting in a burning pain often of the most excruciating nature and associated with excessive tenderness on pressure along the line of the nerve or nerves, and the muscles may be tender on pressure. Formication, numbness, and so forth, may also be present. The trophic changes include glossy skin with atrophy of subcutaneous tissue, and the nails may suffer and the joints become stiff (*vide* p. 113). Among the vasomotor changes are oedema, cyanosis, erythema, and sometimes herpes zoster (*vide* p. 476).

From this brief description of the leading clinical features of ascending neuritis it is clear that they closely resemble those present in forms of neuritis which are not necessarily of the ascending type.

*Prognosis and Treatment.*—The prognosis depends mainly on the

condition of the axis-cylinders and the possibility of allaying the irritation and inflammation by treatment. Modern methods recommended are hot-air baths limited to the affected limb, the use of galvanism, and especially the application of the positive pole to the affected part, high-frequency currents, and sometimes faradism. Massage has been recommended, but it should be applied with the greatest possible care; arterial congestion has also been suggested. Any focus of irritation from an old wound, such, for example, as the presence of cicatricial adhesions, should be removed by the knife. If this measure does not succeed, a portion of the nerve may be excised above or at the seat of pain, and failing this, amputation is probably the only remedy likely to prove successful, and even this has sometimes failed.

**NEUROMA.**—**True neuroma** must invariably contain ganglion-cells, because, with our present conception of the neuron, new nerve-fibres cannot be formed apart from their central ganglion-cells. True neuromas have been described by Virchow, Knauss, Busse, and Loretz, and are practically always found in connexion with the sympathetic nervous system. The recorded cases are very few, and do not call for further comment.

**FALSE NEUROMA** includes all the other varieties, and of these the following forms require special reference:—

#### FALSE NEUROMA

- |   |  |  |                                |
|---|--|--|--------------------------------|
| I. Circumscribed or solitary tumours, growing from the connective tissue of nerve-trunks or of the ganglionic enlargements of nerves. | Innocent   | Fibroma, myxoma, etc. Cysts from liquefaction of solid tumours (myxoma). The clinical type, "painful subcutaneous tubercle," is included here. |                                |
|   | Malignant  | Sarcoma; spindle-celled, fibro-, myxo-sarcoma; cysts from liquefaction of sarcoma.   |                                |
| II. Diffuse overgrowths of the connective-tissue sheaths of nerves and of ganglionic enlargements of nerves. Neuro-fibromatosis.      | <ol style="list-style-type: none"> <li>1. Diffuse and generalised fibromatosis of trunks of nerves ("multiple neuroma").</li> <li>2. Plexiform neuro-fibroma.</li> <li>3. Cutaneous neuro-fibroma (molluscum fibrosum).</li> <li>4. Elephantiasis neuromatosa (pachydermatocoele).</li> <li>5. "Secondary malignant neuroma" being the sarcomatous transformation of one or other of the above.</li> </ol> |  | Various combinations of these. |
| III. Amputation-neuroma.  |  |  |                                |
| IV. Enlargements of nerves in leprosy, syphilis, tuberculosis.  |  |  |                                |

The classification adopted is a modification of that contained in Prof. Alexis Thomson's Monograph on Neuroma.

**Innocent Solitary Fibrous Neuroma.**—These tumours are not always solitary, but they do not tend to implicate the peripheral nerves diffusely, as is the case in neuro-fibromatosis. They are composed of connective tissue, sometimes lipomatous, myxomatous, angiomatous, or lymph-angiomatous, and occasionally contain cysts from softening or haemorrhage. The commoner tumours are fatty or myxomatous, or sometimes a combination of these. They grow in the sheath of the nerve and stretch the nerve-fibres over them. When superficial and related to a small cutaneous nerve they form the "painful subcutaneous tubercle"; when growing on a nerve-trunk they form "trunk neuromas." The chief sites of these painful subcutaneous tubercles are the leg and arm, far the greater number being found in the leg (Wood (50, 51), Courvoisier). They are very common between the ages of twenty and forty, and females suffer more than males. The tumour may be very sensitive, and pain may radiate from it on pressure or when it is exposed to the friction of the clothes. The pain spreads towards the peripheral distribution of the nerve, and sometimes by anastomotic connexions it may enter the domain of a neighbouring nerve. Anaesthesia or paraesthesia rarely results from the presence of such a tumour, and motor disturbance, if a mixed nerve be affected, is also rare. Exceptionally cramps, twitchings, motor paralysis, and even epileptic fits have followed injury to these tumours. The tumour is easily diagnosed, and can usually be shelled out after incision, although in some cases resection and suture of the divided nerve is necessary.

**Malignant Neuroma.**—Sarcoma may be primary in nerves, and may be fibro-, myxo-, or spindle-celled. The growth generally progresses rapidly, and the malignant cells tend to take the place of and destroy the nerve-fibres. The patient is usually in the prime of life, and the clinical evidences of the tumour include pain, formication, cramps, twitching, paralysis, and the resultant wasting of muscles. The great sciatic nerve is the most frequent site of such tumours, and the condition is so malignant that operation is rarely successful.

**Diffuse or generalised neuro-fibromatosis** includes a number of conditions, all or some of which have been called von Recklinghausen's disease. It is extremely difficult to differentiate this heterogeneous group into subdivisions which can be separated from each other either histologically, pathologically, or clinically, but a brief description of each important variety is given.

1. *Multiple Neuro-Fibroma.*—In two-thirds of the cases these tumours are situated on the cranial nerves, especially the vagus. Sometimes one nerve only is affected, sometimes many. The spinal nerves are invariably affected, and occasionally the growths are inside the spinal canal and press on the cord. The anterior and posterior nerve-roots may suffer, and the great nerve-plexuses are often involved; any nerve may be affected,



but especially the intercostals. There may be numerous small cutaneous tumours, and in a few cases the sympathetic and the various ganglia are specially attacked. The endoneurial connective tissue is the chief seat of the pathological process, and the tumour nodules vary greatly in size. Degeneration of the nerve-fibres as the result of the tumour is often present, although some writers deny its existence. There is certainly no new formation of nerve-fibres in the tumour nodules, which are therefore never true neuromas.

2. *Plexiform neuro-fibroma*, described by Verneuil and P. Bruns (27), is composed of nodular and tortuous bunches of nerve-fibres, often matted together by fatty or myxomatous tissue. The wavy nerve-fibres are surrounded and separated from each other by proliferating endoneurium; degenerative changes are accidental, and are certainly not a necessary feature of the tumour (*vide* von Bünger, Delore and Bonne.) The nerves of the skin and subcutaneous tissue are usually affected, but the lobulated masses may penetrate deeply and may even become adherent to the bones. The condition begins in fetal life and is generally connected with a branch of the trifacial nerve in the orbit or upper eyelid. Another site for this rare tumour is on one of the branches of the cervical plexus in the neck or behind the ear, but it occurs also in connexion with nerves of the extremities, of the breast, and occasionally the back, or even the tongue (Abbott and Shattock). The skin over the tumour may be healthy or may be infiltrated with a new growth of connective tissue.

3. *Cutaneous Neuro-fibroma* or *Molluscum Fibrosum*.—This is the special form of diffuse neuro-fibromatosis which was first called von Recklinghausen's disease. It must, however, be remembered that all cases of diffuse neuro-fibromatosis, whether belonging to this particular type or not, may shew pigmentation, the sensory and motor phenomena, and even the less common mental peculiarities which von Recklinghausen described as characteristic of the disease to which his name has been given (Feindel). The essential features are as follows: (i.) numerous small soft fibrous nodules, some sessile others pedunculated, varying in size from a millet-seed to a small nut, situated in the thickness of the skin. There are sometimes larger cutaneous or subcutaneous tumours which may belong to the type of plexiform neuroma. The structure of the nodules of this type closely agrees with that of plexiform neuro-fibroma. (ii.) Tumours on the nerve-trunks occur in a large proportion of the cases. The superficial tumours are palpable, those on the nerve-trunks and situated centrally generally give rise to marked phenomena such as pain, cramps, contracture, and paralysis, and are thus easily recognised. These tumours may grow rapidly, may vary greatly in size, and usually certain of those superficially and also of those deeply seated are, as already stated, of the nature of plexiform neuroma; in other words there is a combination of the second and third types. (iii.) Pigmentation of the skin occurs in about half the cases, sometimes in small spots, sometimes in larger patches. The former are found on the trunk and the upper



part of the limbs and are not generally met with on the face, hands, or feet. The patches are of a brownish-white colour and vary greatly in size. The small pigmented spots may disappear, the larger patches generally persist. Ordinary naevi are not uncommon in the subjects of this disease. (iv.) There are many sensory and motor phenomena due to the presence of the neuromas, such as pain, paralysis, contracture, cramps, and weakness of the muscles. Pain is generally the result of pressure, but sometimes the rapidity of growth and consequent infiltration of the nerve-fibres may cause agonising pain even lasting for hours. Pain localised in the cervical spine and in the region of the cauda equina may be due to deeply-seated tumours.

In addition, there may be peculiar mental changes which are said to be characteristic; they include gradual loss of intellectual power and marked despondency. Some cases depart more or less widely from this description. The disease is, as a rule, congenital, and is sometimes hereditary.

The prognosis should be guarded. It depends on the possibility of operative treatment, which is by no means always satisfactory, although some tumours causing pain or inconvenience can be removed; nerve section or even amputation of a limb has sometimes been preferred.

4. *Elephantiasis Neuromatosa*.—Virchow differentiated a form of elephantiasis which involved specially the nerves of the part. There is an extremely widespread connective-tissue invasion not only of the skin, the subcutaneous tissue and the muscles, but also of the nerves of the part in a way closely resembling that seen in multiple neuro-fibroma. This change is, as a rule, confined to one limb or part of a limb or to one part of the body such as the scalp. Pain is generally absent, and the case resembles one of ordinary elephantiasis. There may be a considerable amount of pigmentation of the skin in these cases.

5. *Secondary malignant neuroma* is simply a sarcomatous transformation of one of the preceding types of tumour, and does not demand any special description.

**Amputation-Neuroma.**—After an amputation, larger or smaller bulbous swellings form on the proximal ends of the divided nerves. These swellings are the expression of the enormous vitality and rapidity of growth of divided axis-cylinders in their efforts to reach the structures to which they were formerly distributed. The funiculi grow beyond the point of section, are arrested in their efforts to grow straight onwards, and, partly by the thickened perineurium and interstitial tissue between the funiculi and partly by other causes, become twisted into a bulbous swelling. But though the funiculi are arrested in their growth, the individual axis-cylinders continue their efforts; and many of these can be seen isolated or in little groups of two or three, making their way amongst the strong bands of connective tissue. The recent observations on the regeneration of the neuro-fibrillae, of which the axis-cylinders consist, are described in a previous article (p. 189). Sections taken from the neuroma, and at short intervals above it, give an admirable picture

of "ascending degeneration" in the nerve, especially if a number of nerves, obtained at varying dates after amputation, can be examined. A few fibres have degenerated to some extent upwards; these are fibres whose chief trophic centre appears to be situated peripherally: they are few and far between, and some doubt has been expressed as to their existence. The majority of the larger fibres in the stump of a mixed nerve merely become thinner, less well covered with myelin; yet they persist as definite nerve-fibres. But the most striking change is seen in the fine fibres, which are in all probability mainly vasomotor in function. Those which have lost their function—those, that is, passing downwards to vessels in the nerves or tissues below the level of division of the nerve



FIG. 64.—Funiculus of rabbit's sciatic nerve, healthy side, shewing fine medullated fibres in groups or strands.

—have degenerated, and their place is taken by connective tissue. This can be seen very clearly, because these fine fibres in a healthy mixed nerve are all, or nearly all, medullated; and, further, they are grouped together in the funiculi, and hence are readily recognised. Above a neuroma after amputation the place of these fibres is taken by connective tissue, and on microscopical examination these patches are very definitely seen. As the nerve is investigated farther upwards these fine fibres become less affected, because at a higher level there is an ever-increasing number of fibres whose function is still retained.

Further than this, one striking change in the vessels, which appears to be associated with the degeneration of the fine fibres, is well demonstrated. Where the fine fibres have degenerated the vessels shew marked proliferation of the nuclei of the intima, to a less extent of the media,

and to a still less extent of the adventitia. This proliferation of nuclei is well seen in the capillaries, arterioles, and venules; and it appears to decrease as the nerve is examined farther and farther upwards, away from the neuroma. It seems possible that the connective tissue replacing the degenerated fine medullated fibres, which have lost their function, may by compression have damaged neighbouring fine fibres, and so have produced, though to a gradually diminishing degree, this remarkable change in the vessels. The fact that in many cases of toxic neuritis three events are present—namely, early degeneration of these fine medullated fibres, proliferation of nuclei in the vessels, and exudation of lymph with lymphoid cells and sometimes red blood-corpuscles—seems to indicate

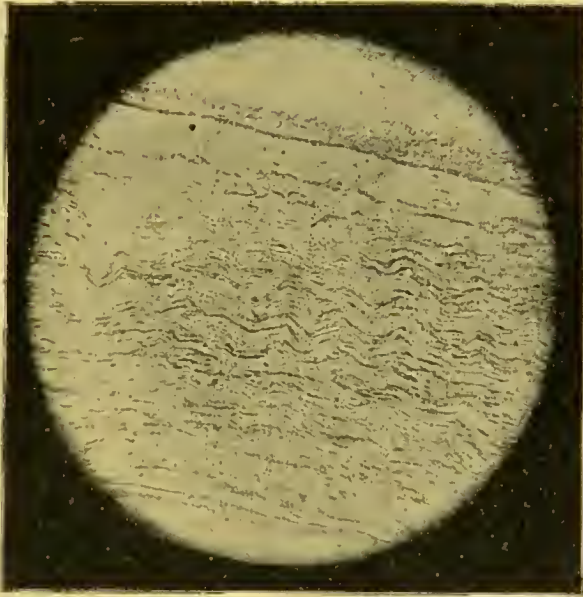


FIG. 65.—Funiculus of proximal end of rabbit's sciatic nerve, twenty-three days after application of a double ligature, shewing thickened connective-tissue septa replacing fine medullated fibres.

that the fine fibres and the vessels are associated, and that they play an important part in many nerve-diseases. It only remains to be stated, that there are more nerve-fibres in the neuroma itself than there are entering it; and this notwithstanding that the twisting of the fibres adds apparently to their number, and that many fibres are so compressed by fibrous tissue as in all probability to be arrested in their further growth. The cause of this is that the old nerve-fibres, or as many of them as are able to do so, proliferate; and each old axis-cylinder may give origin to several young ones, which rapidly acquire myelin sheaths.

*Symptoms.*—An amputation-neuroma becomes pathological when it causes pain and discomfort. The pain is sharp, burning, or shooting; and is specially severe when any pressure is exerted on the neuroma. The pain may thus prevent the use of an artificial limb. In addition to



sensory phenomena there is sometimes twitching or actual muscular spasm; and, as such phenomena are produced reflexly, they may be unilateral or bilateral. Even epileptic seizures have followed the irritation of such a neuroma; and, though rarely, profound mental depression may be caused by a painful neuroma.

The *prognosis* of such a case is not entirely satisfactory; operation will temporarily relieve the condition, but it may recur in course of time; much undoubtedly depends on the care taken by the surgeon.

The *treatment* is simply removal; and in so doing to make every effort to prevent inflammation in the stump, and to cause the formation of as small a bulbous end to the nerve as possible, and in a situation where it may escape most pressure.

*Syphilis* frequently affects the cranial nerves, but generally within the skull; and much more rarely attacks spinal nerves. Where spinal nerves do suffer, the inflammation is generally secondary to syphilitic inflammation of the spinal meninges, and it is the nerve-roots which are the site of syphilitic exudation. In this way one or more nerves may become affected. A gumma may by chance involve a peripheral nerve, and occasionally interstitial inflammation in a nerve may be of syphilitic nature; but such cases are rare. These forms of syphilitic affection of nerves are secondary or tertiary. No special anatomical description is requisite, and the symptoms and signs are in no way different from a local neuritis. The *diagnosis* will depend mainly upon the history of the case and coexistent evidence of syphilis. The *prognosis* is favourable in many cases, in which early treatment is possible. The *treatment* consists in the administration of iodides and mercury, both together or alternately. These remedies act marvellously; and where there is any evidence of an acute, or what is more common, a subacute inflammatory process, mercury is invaluable (*vide* also p. 440).

**PRESSURE ON NERVES.**—Every one is familiar with the “pins and needles” sensation, and most people with the inability to co-ordinate, or even in any way to put the affected muscles into motion, which follows prolonged pressure on a mixed nerve. Pressure, not in itself severe, will in time produce the familiar sleeping foot; or the more lasting paralysis of the upper extremity of the drunkard who falls asleep with his arm hanging over a chair; or the well-known crutch-palsy of the cripple. The prickling begins with either a hot or cold sensation, and it passes away as soon as the pressure is removed. When a nerve in an animal is ligatured, the distal part swells rapidly, often increasing to three times its former size; and, if the ligature is retained, this swelling persists and even increases for a long time. Is it not possible that pressure, in no degree approaching the severity of a ligature, may yet interfere with the circulation of blood or lymph in the peripheral part of a nerve? Pressure at least interrupts the conduction of nerve-impulses, and moreover by its irritation causes very distinct paraesthesias or perverted sensations. Pressure must therefore break the nerve-currents in



some way, and it certainly generates currents of a remarkable kind, passing sometimes in the direction opposite to their ordinary route. This is difficult to explain, although there is some plausibility in the suggestion that as myelin is in a fluid state during life, any displacement of its molecules may interfere with its function as an insulating medium for the axis-cylinders; but this hypothesis does not materially help us to understand the problem. In seeking for a workable explanation it certainly seems very much easier to take into account the disturbed circulation of blood or lymph.

In a case in which there is prolonged pressure on a mixed nerve, as in crutch-palsy, the motor paralysis is far more marked and more prolonged than the sensory. With almost complete paralysis, after the prickling feeling has passed away, there may be no lasting sensory change at all; or some formication may continue without actual loss of sensation, common or tactile. Perhaps this well-known symptom of pressure-paralysis is one of the strongest arguments in favour of a dual trophic centre for most sensory fibres, if not for all. If there is a trophic centre in a touch-corpuscle, and a greater trophic centre in a cell, either of a posterior-root ganglion or of the cord, surely these sensory fibres should recover with greater rapidity, and just in the same way be more capable of rapid union and early resumption of function after suture of the two ends of a divided nerve?

Lastly, the result of pressure on a nerve depends greatly on the vitality and general state of health of the individual. The slightest pressure kept up for a short time on a nerve, which in health would not produce any effect, in a person debilitated by some illness may cause marked paralysis.

*Etiology.*—There are many causes of pressure; a complete list would necessitate a consideration of most of the nerves of the body separately. Besides pressure from without, instances of which have already been referred to, dislocations, fractures, and tumours of all kinds are among the common causes of pressure from within.

*Morbid Anatomy.*—Much of what has been said above might be repeated here. Pressure kept up for a short time only causes transient symptoms and signs, probably dependent on changes interfering rather with the functions of the nerve than with its anatomical structure. But prolonged pressure is apt to set up distinct local exudation, with subsequent organisation into connective tissue, constituting a form of interstitial neuritis; or it may, though much more rarely, cause the parenchymatous form. But it is quite possible for pressure to interrupt all nerve-impulses completely, to divide the nerve as by a ligature, without any real inflammatory process at all. This, however, is extremely rare.

The *symptoms* vary greatly, as the pressure is slight and persistent, or sudden and severe. Where the pressure is very gradual, as from the growth of a tumour, there is an extraordinary power of resistance in nerve-fibres, and a capacity for adapting themselves to altered conditions; always provided that the pressure be exerted slowly enough. Every one

is familiar with instances of tumours apparently pressing on nerve-fibres but not causing any symptoms. Less gradual pressure, as by the finger on a nerve, and where there is no opportunity for the nerve-fibres to adapt themselves to the compressing force, causes tingling in the area of skin supplied by the nerve, and a peculiar hot feeling; later anaesthesia or paraesthesia sets in, and then loss of motor power and of co-ordination in the affected muscles. When the pressure is removed, motion and co-ordination in the affected muscles are regained, and sensation returns. The tingling may last for a longer time; but any protracted alteration in function implies either a definite nerve-fibre lesion or inflammation resulting from the pressure. As already stated, the health of the individual determines the early appearance, the severity, and the duration of these sensory and motor phenomena; the slighter pressures causing more marked results in debilitated than in healthy subjects.

It must be remembered that in the palsied arm of the drunkard, who falls asleep with the arm hanging over the back of a chair, anaesthesia and motor paralysis may last for hours or days; implying a more severe interference with the conducting power and the molecular structure of the nerve at the site of pressure. There is most probably interference with the circulation of blood and lymph in the nerve, and thus is set up the condition which, in effect at least, is a local neuritis. Gradual recovery is the rule, even though a certain amount of atrophy of the affected muscles may have occurred.

The *diagnosis* should depend on the nerve affected, and whether it be one which is liable to compression. Generally a history of compression is obtainable, but each nerve requires separate consideration in this respect.

The *prognosis* is usually favourable; although, in many cases, days or even weeks may elapse before sensory and motor power return.

The *treatment* is exactly the same as in nerve injuries, but suturing is unnecessary, unless the compressing force has caused complete division, or a fibrous nodule has formed at the site, preventing regeneration. Massage, electricity, and passive movements are indicated, care being taken to ensure rest so long as there is any active inflammatory process in the affected nerve.

**WOUNDS OF NERVES.**—A nerve may be injured in many ways, especially by cuts, stabs, or gun-shot wounds. The median and sometimes branches of the ulnar nerve are injured by such accidents as occur in aerated-water factories, or in work with sharp tools. The effect of a lesion depends, first, upon the magnitude of the nerve or the nerve-trunk damaged; secondly, and more especially, upon the amount of bruising and laceration; and, thirdly, and perhaps most important of all, upon the presence or absence of infective organisms. The larger the nerve which is injured the more likely are serious consequences to ensue. The most serious result is undoubtedly progressive ascending neuritis. It must, however, be remembered that a nerve, after division,

may unite by first intention, provided there be nothing to interfere with such union.

The division of a large nerve, such as the sciatic, is serious for three reasons: first, because it means a deep wound, and therefore almost certainly much bruising and inflammatory lymph; secondly, because when a large nerve is injured, an extensive area of the body is cut off from the central nervous system; and lastly, the shock caused by the injury to a large nerve-trunk is extremely great; fainting is by no means uncommon; indeed, in a weak subject even fatal syncope may occur. The sciatic nerve is more frequently injured in warfare than in times of peace; but the scythe has been responsible for not a few accidental sections.

The *anatomical* changes resulting from a nerve injury depend much on the nature of the case. A full description of the changes following division will be found on p. 187 *et seq.*

A neuroma may form on the extremity of the proximal end, of the nature of the amputation-neuroma already considered. The amount of inflammatory exudation, or haemorrhage, in the neighbourhood of the divided fibres will greatly influence the future history of the case. A large amount of bruising, as in a gun-shot wound, means a great exudation of inflammatory lymph, probably haemorrhage, and a proportionately more difficult task for the severed nerve-fibres which are endeavouring to reunite. The presence of an infective organism implies the grave risk of ascending neuritis; and a large amount of organised lymph or blood-clot will undoubtedly hinder reunion of the nerve-fibres, and, by pressure on the proximal end, may keep up persistent irritative action, which, although certainly local, has been called a form of ascending neuritis.

The *symptoms* depend on the nature of the individual case. If a mixed nerve be completely divided there will be paralysis of motion and sensation in the affected part, with—unless union occur by first intention—well-marked reaction of degeneration. If the union be by first intention the reaction of degeneration may be partial or incomplete.

At the moment of the accident, if a large nerve be divided, there is frequently severe shock with faintness; and this may be increased by intensely agonising pain following on the injury, and only gradually abating.

Weir Mitchell (66) describes the sensations of a gun-shot wound as varying markedly; of 91 cases, investigated by him, in fully one-third there was no pain, although a nerve was known to be injured by the bullet: in such cases the sensation resembled a stroke with a stick, or was unperceived till the bleeding directed attention to the wound. In other cases there may be intense pain and faintness. Where a nerve is not completely divided there may be a spasm of muscles. After a complete division of a nerve there is anaesthesia; when it is partial there is often hyperaesthesia in the area of the skin involved, and the pain felt along the line of the affected nerve is of a burning and intensely agonising kind.



If the injury does not amount to division, very often there is more marked motor than sensory paralysis; and the sensory fibres appear to recover far more rapidly than the motor. This may indicate greater vitality, and consequently more rapid recovery of sensory fibres; or that sensory impulses require less perfectly insulated nerve-fibres; or, lastly, that there may be anastomosis to some extent with sensory filaments of neighbouring nerves which are able to take the place of the damaged fibres. Certainly after a severe bruise of a nerve there may be motor paralysis, and extreme hyperaesthesia of the affected muscles when they are grasped, or stimulated to contract by electrical currents.

The electrical reaction of the affected muscles is that of degeneration. There is loss of reaction in both nerve and muscle to the faradic current (after complete division); and the irritability of the muscle to the galvanic current fails coincidently with the loss of irritability of the nerve. But in ten days to a fortnight the irritability of the muscle to the galvanic current becomes rapidly increased, till it far exceeds the normal; the well-known polar changes occur, and moreover, and perhaps of greater import, the character of the contraction alters: it begins more gradually, lasts much longer, and can be produced with a much weaker current. Where the nerve lesion is not recovered from, the increased galvanic irritability of muscle persists for a number of weeks, and gradually disappears with the increasing atrophy of the muscle-fibres. It must be remembered that in many cases, in which a nerve is slightly injured, both nerve and muscles may be induly irritable to both kinds of electricity, and especially to the faradic. As the reaction of degeneration proceeds, however, the muscles first become flabby and then waste; and their recovery depends on the restoration of continuity in the motor fibres conducting trophic impulses. With the abolition of sensation and of motor power the reflex arcs belonging to the affected area are abolished.

The vasomotor and trophic changes in a severe case are very well marked, and are described on p. 112 *et seq.*

The *diagnosis* is not difficult, as the symptoms of either a slight or a severe nerve injury are distinctive, and the restricted area of the lesion defines such a nerve injury from multiple or toxic neuritis, should the history of the case permit of any doubt.

The *prognosis* is most important, because it is sometimes possible, by a careful examination of the affected limb, to predict the probable duration of the effects of the injury, and the ultimate result.

After the diminution in irritability of the nerve to the faradic current, which usually immediately follows a nerve lesion, accompanied as it is by a similar fall in excitability of the muscle to both currents, the continued preservation of faradic stimulation in the nerve and muscle is a good sign, indicating that the nerve-fibres can still conduct. Incomplete quantitative and qualitative changes in the affected muscles to the galvanic current can be also construed into a more hopeful prospect of speedy recovery. The reappearance of reaction to the faradic current, both in nerve and muscle,



always indicates restoration of conduction of nerve-fibres; although the galvanic changes, qualitative and quantitative, may still persist in the muscles for a long time after regeneration, and after the gradual return of conducting power has begun.

The *treatment* closely resembles that recommended for local neuritis. The first steps are rest to the affected part, reduction of inflammation, and the cleansing of any septic wound, should the injury have caused such a condition.

Where nerves have been severed by a wound, care should be taken to bring the divided ends into apposition, by suture if necessary. When time has been allowed to elapse without union of the divided nerve, an operation should be performed, the ends of the nerve being rawed, and brought together by suture. It is often difficult, after the lapse of months since the injury, to distinguish the peripheral end; but the removal of the bulbous extremity of the proximal end, and its union to the remains of the peripheral end, which may be mostly connective tissue, will often suffice to effect a complete regeneration of the peripheral part of the nerve.

Bowlby, Willard, and others have collected statistics of primary suture of nerves, and, considering the number of septic wounds which had to be included in the tables, these are very satisfactory. Mr. Bowlby records 81 cases; of these 32 were successful, 22 were partially successful, 12 doubtful, 14 failed, and the issue of one was unknown. The sutures commonly recommended are sterilised silk or catgut. There is some difference of opinion whether the suture, generally of catgut, should be passed through the nerve or simply through the sheath. The main object is to bring the two ends into accurate apposition, and to do so with as little handling of the nerve, and certainly with as little squeezing of the nerve with forceps as possible. On no account should the nerve be gripped, but the forceps should always be used simply for picking up the sheath of the nerve and steadying it when introducing the stitch. After the operation, the part should be kept absolutely at rest, and a splint is very desirable. As soon as possible, massage to the affected muscles should be commenced; and electricity, especially at an early date galvanism, and later, when the muscles react, faradism, should not be neglected. The patient should be warned about the risk of injury to the affected skin, and specially as to burns with warm water.

Secondary suture is the term applied to bringing into apposition the ends of the divided nerve at a date later than the first twenty-four hours. In this case, as a general rule, the proximal and peripheral ends of the divided nerve have to be rawed before being brought into apposition by a careful suture. This presents no difficulty when the operation is undertaken within a limited time. Where, however, the peripheral end of the divided nerve is practically reunited by a band of connective tissue difficult to distinguish from surrounding structures, and, what is of more importance, when there is evidence that regeneration of the peripheral end is impossible, operation should not be lightly undertaken. If the nerve is

a mixed nerve, any evidence of galvanic irritability should be carefully sought for in the affected muscles, and the results of the lesion, such as contracture of joints and alteration of tendons, should be investigated. Dr. Head and Mr. Sherren point out that in cases in which trophic ulcers are present, although it may be impossible to ensure any definite return of epieritic sensibility or motor power, restoration of the trophic fibres for the skin by secondary suture is well worth consideration. In cases of secondary suture, and more rarely in primary, it may be impossible to bring the ends of the divided nerve into apposition. In these circumstances, one of three procedures should be attempted: (i.) A portion of nerve from an animal, or from an amputated human limb, or part of a nerve removed for the purpose from the patient himself, may be introduced into the gap. Apparently human nerve is preferable to a nerve obtained from an animal, but naturally the risk of infection and the practical difficulty that it is not always possible to procure a suitable portion of nerve; renders this procedure unsatisfactory. The nerve introduced must be absolutely fresh, and be removed as speedily as possible from the one part to the other. (ii.) A better plan is to use some channel of communication along which the proximal nerve-fibres may reach the peripheral end of the divided nerve. Such a channel of communication may be formed from decalcified bone, from a piece of an artery of an animal or man, or, perhaps best of all, a portion of a subcutaneous vein removed from the patient himself. The tube so formed is pulled over the ends of the nerve, which must be secured to each other by catgut sutures; the tube in a way helps to bridge over the gap, but when there is a gap of more than three inches this operation is very unlikely to be successful. (iii.) Anastomosis may be carried out in several ways. A neighbouring healthy nerve may have the peripheral end of the divided nerve either (*a*) introduced into a slit in its trunk; or (*b*) introduced into a flap-like opening made in its trunk; or (*c*) after a part—a third or a half—of the normal nerve has been slit up for a certain distance, the peripheral end of the divided nerve is sutured to the free half; or (*d*) the affected nerve may be divided and a part of it introduced into the neighbouring healthy nerve; or (*e*) the healthy nerve may be completely divided and its proximal end introduced into the peripheral end of the divided nerve. This last method is eminently undesirable. As a third, or even more, of a healthy nerve may be divided without producing changes either in sensation or motor power, it is clear that anastomosis is not such a serious operation for the healthy nerve as might be anticipated. Generally there is no initial increase of anaesthesia or paralysis, and the trunk of the healthy nerve is soon able to deal with the new area of distribution in addition to its own; sensation and motor power return very successfully, but much depends upon the duration of the lesion.

It has been suggested that by removing a piece of bone the affected limb might be shortened, and so the ends of the divided nerve might be brought into apposition.

Lastly, reference should be made to the method originally recom-



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mended by Letievant. He prepared two flaps, one from each end of the nerve, and bending them back, formed them into a bridge over the gap. This operation is extremely likely to be followed by the formation of a neuroma and failure in perfect conduction of sensory and motor impulses.

*Results of Operation.*—After a period during which there is no return of either sensory or motor functions, there follow, according to Dr. Head and Mr. Sherren—(i.) restoration of protopathic sensibility which takes six to sixteen weeks to commence; this variable period depends upon the age of the patient, the nerve injured, and, of course, the nature of the wound. (ii.) The second stage is characterised by the return of sensibility to light touch and minor degrees of temperature. Here again the period is variable, any delay being due to the same causes as in the first stage. The further the lesion is from the periphery, the longer will be the process of recovery, and the more delayed will the different stages be. It may therefore be stated that the second stage should begin possibly as early as the sixth week, but more likely as late as the fortieth, and may not be complete until about the seventy-fifth week. (iii.) The third stage follows and implies restoration to light touch and minor degrees of temperature, and may be examined by means of the compass and other tests. Complete recovery may not occur till one and a half, or even more, years have elapsed, and may not occur at all.

Recovery of motor power varies considerably, and generally follows considerably later than the first stage of sensory restoration. It also depends on the age of the patient, the distance from the periphery of the site of the lesion, and the nature of the wound. It often takes one, or even two years, for restoration to take place. Certain muscles recover earlier than others. According to Etzold, if the ulnar nerve is divided at the elbow, the flexor carpi ulnaris recovers at a much earlier date than the intrinsic muscles of the hand, which take, as a rule, about two years. Section of the nerve at the wrist will probably be followed, if primary suture is performed, by a restoration of motor power in a year, whereas under similar conditions section at the elbow takes double that time. Usually the time required in cases of secondary suture is nearly double that required in primary. Mr. Bowlby states that a limit of two years after the primary lesion renders the final complete recovery of motor function almost impossible, and he gives four years as a period which has never been exceeded in any recorded case in which motor power was regained to anything like a perfect degree.

Where pain becomes excessive after secondary suture, the wound should be reopened and any adhesions or probable cause of the pain investigated.

## GROUP II.—SPECIAL AFFECTIONS OF THE SPINAL NERVES

Under this head fall the individual affections of the different nerves. It will be convenient to review the diseases of the nerves of the trunk in the first place, and of the limbs afterwards.

The accompanying table of the spinal segments and their nerves and

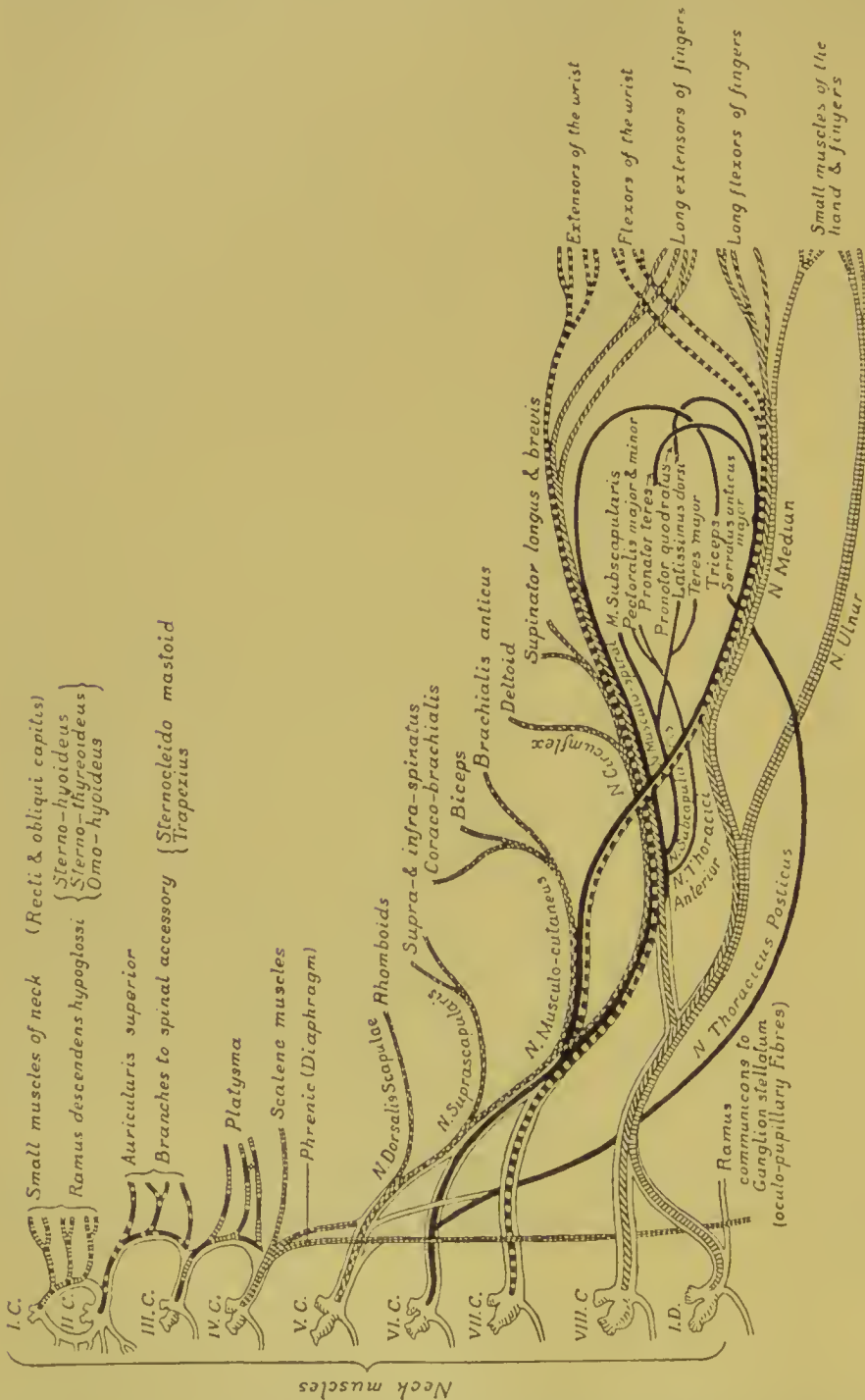


FIG. 66. Diagram of the motor nerves derived from the cervical and first dorsal nerves.

muscles has been compiled partly from original investigations, and partly from the results of previous observers, more especially Sir W. Gowers and



*Causes.*—A carious tooth, pressure of a heavy load, or a severe blow on the neck, caries of the upper cervical vertebrae, cerebrospinal meningitis, infective diseases such as influenza or malaria, cold, gout, and rheumatism are all included in the category of causes producing this form of neuralgia. The subjects of anaemia, persons of a nervous or hysterical disposition, and convalescents after a severe attack of some continued fever, such as influenza or enteric, are specially susceptible.

*Clinical History.*—There is generally a persistent dull pain, with acute lancinating paroxysms. It is generally bilateral; and there are the usual tender points, the more common, according to Valleix, being—(a) where the great occipital nerve emerges between the mastoid and the spine of the first cervical vertebra; and (b) at the posterior border of the sternomastoid muscle, where the occipital nerves are grouped together; (c) a parietal point near the top of the head; and (d) a point over the mastoid process. Movements of the head, such as are caused by walking rapidly, or sneezing, increase the pain, and the head is generally held somewhat stiffly. In some cases the cervical glands swell and become painful, and over the affected region of the scalp there may be hyperaesthesia of the skin, or even falling out of the hair; there may also be tenderness on pressure between the shoulder-blades in the supraclavicular fossae.

Not infrequently trigeminal neuralgia accompanies this form, and the first and third branches are especially involved.

*Diagnosis.*—It is not difficult to distinguish this form of neuralgia from rheumatism, because the pain in the latter is generally worst at night when the sufferer becomes warm in bed, and the area over which pressure is painful is much more extensive than the tender points in neuralgia.

In hysteria there may be severe pain in this region, but the mental element in the case and the painful points differ distinctly.

The *prognosis* depends much on the patient. In older persons the condition may resist treatment for a long time, or may be intractable, and may even render the patient's life almost unbearable. In other cases the prognosis is much more favourable.

*Treatment.*—General treatment for neuralgia; but counter-irritation is of great value, and hence Paquelin's cautery, or the button cautery, applied on either side of the spinal column in the cervical region, is often most efficacious. In one case the superior cervical ganglion of the sympathetic and the cord below were fixed by adhesions; on freeing the sympathetic by operation, the patient's symptoms, including the cervico-occipital neuralgia, disappeared (Johnson).

**Neuralgia of the Phrenic Nerve.**—The phrenic nerves arise from the fourth, and possibly also the third, cervical roots.

*Causes.*—Neuralgia of the phrenic is rare. It is associated with diseases of the heart, pericardium, and large vessels; or it may be due to local irritation, as from a fractured clavicle (in one recorded case), or a mediastinal tumour.

*Clinical Features.*—The pain shoots upwards from the region of the



diaphragm to the throat or shoulder of the affected side, and generally it is the left phrenic in which the neuralgic pains occur. Breathing may be painful, especially if both sides are involved, which, however, is rare.

*Diagnosis.*—The pain closely corresponds to angina pectoris of organic origin; indeed it may be a form of that complaint, and be brought about by the same causes, rendering a differential diagnosis extremely difficult.

*Prognosis.*—This is good, provided there is no evidence of organic or vascular disease, and the neuralgia is either purely functional or due to a removable or curable cause, such as fracture of the clavicle.

**Paralysis of the phrenic nerve** may be unilateral or bilateral. If the former, there is often some difficulty in recognising the existence of the paralysis.

*Etiology.*—Lesions of the cervical cord, of its membranes, or of the nerve-roots (3rd or 4th cervical) may cause the condition. These include hæmorrhage, pachymeningitis, syphilitic meningitis, and, not uncommonly, fracture or disease of the spinal column. The phrenics are occasionally paralysed in tabes. Wounds or tumours of the neck or thorax may injure or compress the nerve. In diphtheritic neuritis, and less commonly in beriberi, the phrenics may suffer; and in toxic polyneuritis (alcohol, lead, carbon monoxide, etc.) these nerves are frequently affected. I have seen some cases of alcoholic neuritis in which implication of the phrenics along with the intercostals has been the immediate cause of death. Although Sir W. Gowers is inclined to regard cold as a possible agent in the production of phrenic neuritis, it is more probable that cold is not the sole factor, but that it acts in conjunction with some other, such as alcohol. The branches of the phrenic nerve in their distribution to the diaphragm may be affected by pleurisy or peritonitis. Lastly, hysterical paralysis of the diaphragm sometimes occurs.

*Symptoms.*—A unilateral paralysis does not cause any special inconvenience to the patient. Bilateral paralysis implies loss of diaphragmatic breathing, and even with the deepest inspiration there is no protrusion but rather retraction of the abdomen. Litten's diaphragm phenomenon in a normal individual is an undulatory movement of the interspaces, which descends from the sixth interspace downwards for several interspaces during deep inspiration (*vide* Vol. III. p. 1002). This disappears in paralysis of the diaphragm.

The breath-sounds at the bases are feeble, and there is a great tendency to engorgement, especially of the lower lobes, and also to bronchitis. Dyspnoea is not well marked except on exertion, unless advanced pulmonary engorgement already exists, when the dyspnoea may be so severe as to amount to a feeling of suffocation. Coughing is very difficult, and the abdominal pressure required for assisting the evacuation of the bladder and bowels cannot be exerted. In neuritis there are often painful points over the scalene muscles or between the bellies of the sterno-mastoid muscle.

*Diagnosis.*—Diaphragmatic breathing is often in abeyance in hysteria, and in any case women do not use it much except on exertion. A useful

test in such cases is more or less violent exercise, when, unless paralysis exist, diaphragmatic breathing must be evident. In pleurisy, especially diaphragmatic pleurisy, pain may prevent any movement of the diaphragm; and in those rare cases in which the muscular fibres of the diaphragm undergo degeneration, some difficulty may be experienced in deciding whether there is a nerve or a muscle lesion.

*Prognosis.*—In diphtheritic neuritis and beriberi, phrenic neuritis will probably terminate fatally; and in alcoholic multiple neuritis the implication of the phrenics is very frequently of grave import. In rheumatism and in most cases of hysteria a favourable opinion can be given. In other cases, due to aneurysm or tumour, the nature of the disease and the possibility of relieving the condition by operative or other interference, must govern our opinion.

*Treatment.*—Where treatment is possible, the essential point is to treat the cause by removing a tumour, if one exist; or by combating the toxic element in the case. Neuritic inflammation may be attacked by counter-irritation over the lower and inner parts of the anterior triangle of the neck, as advocated by Dr. Suckling. Hypodermic injections of strychnine have been used with advantage in diphtheritic cases. The phrenic nerves may be stimulated by either faradic or galvanic currents, the poles being pressed firmly one on either side of the neck just behind the sterno-mastoid muscles. In polyneuritis galvanism may be cautiously applied, and later faradism.

**Neuralgia of the Intercostal Nerves.**—The second down to the ninth or tenth dorsal nerves are most commonly affected, and more frequently on the left side.

*Etiology.*—This affection is very common in women, both in adolescent and adult life; it is proportionately much less frequent in men; in old persons of both sexes it is found fairly equally.

Anaemia, cachexia, leucorrhoea, exhaustion following on lactation, severe illness, especially fevers, sexual excess, and similar factors not uncommonly cause the condition. Local injuries may also be responsible for not a few cases, such as a blow or injury over the thorax, fracture of one or more ribs (especially if reunion occurs with a large formation of callus directly interfering with the intercostal nerves), scoliosis, or other disease of the vertebral column, and possibly pleurisy. But intercostal neuralgia may be reflex; and probably the frequency of its occurrence on the left side in angina pectoris, actually constituting in some cases the anginal attack, is a proof of this reflex irritative action. In aortic aneurysm, however, the sac may directly press on one or more intercostal nerves.

*Clinical History.*—The pain is dull and constant, with occasional sharp lancinating paroxysms. Sometimes, though rarely, the pain is spasmodic, appearing to shoot through the chest; and the spasm is relieved only by a deep breath or other effort of the thoracic muscles.

The tender points are distinctive, corresponding to the three cutaneous branches—posterior, lateral, and anterior—of the intercostal nerves;

although one or two of these are specially sensitive, the nerve-trunk is very rarely painful all along its course. The affected skin is not infrequently hyperaesthetic, and even the pressure of the clothes may be unbearable. Herpes zoster is common, and the neuralgic pain may anticipate the herpetic eruption, and also continue long after it has disappeared (*vide* p. 480).

*The diagnosis* is generally easy; care should be taken to examine the condition of the heart, lungs, pleurae, the breasts in women, and the spine.

*The prognosis* is generally favourable, although in some cases the pain persists for a long time. The heart, aorta, pleurae, and spine should be examined before the probabilities of final and complete recovery can be estimated.

*Treatment*.—Counter-irritation, as by fly-blisters, mustard, or the button cautery, is of great value. Where herpes zoster is associated, sedatives must be used. Tonics are generally indicated, and any irregularities of the alimentary tract should be rectified. Galvanism has been successful in one or two cases, but it is rarely of much benefit. The article on trigeminal neuralgia should be consulted for internal and topical treatment (p. 566). Nerve section or section of the sensory roots should not be considered until all else has failed. Where callus presses on the nerve it should be removed.

**Neuralgia of the Breast; Mastodynia.**—This curious form of neuralgia involves the branches of the intercostal nerves supplying the skin of the breast (2nd-6th), or the gland structure itself (4th-6th).

*Etiology*.—The condition is met with in women almost exclusively, and generally about middle life. It is associated with excessive stimulation of the breast, as in over-lactation, or in pregnancy; but not infrequently it occurs in anaemic, neurasthenic, or hysterical women, without any functional activity of the affected gland at all, although in these cases it is generally more severe during menstruation. Tubercula dolorosa have been found on the nerves supplying the gland structure. Lastly, it may occur as the result of a neoplasm of the breast.

*Clinical History*.—The pain is sharp, and more often found on the left side; there may be circumscribed redness and swelling of the breast. Occasionally milky fluid exudes from the nipple (Erb), and herpes may be associated with the condition. The tender points are generally near the spinous processes of the vertebrae (2nd-6th dorsal).

*Diagnosis*.—The existence of a neoplasm can readily be recognised, especially if it be malignant, by digital examination, and so the swelling resulting from mastodynia alone can hardly be a source of error.

*The prognosis* depends almost entirely on removal of the cause, and the degree of benefit obtained from treatment. In many cases the condition is very intractable.

*Treatment*.—Attention must be paid to the general health, and any obvious cause such as excessive lactation must be dealt with. Supporting the breast by a bandage, the application of soothing liniments, painting



the nipple with a strong solution of cocaine, and the constant current are all useful.

**Brachial Neuralgia.**—The brachial plexus is derived from the four lower cervical and the first dorsal nerves, with sometimes a branch from the fourth cervical. The neuralgic pain may affect all the nerves of the plexus, or may be limited to one or two alone; not infrequently other nerves, such as the intercostals, or even the fifth cranial nerve, suffer in sympathy.

*Etiology.*—There are generally predisposing causes, such as anaemia, debility, neurasthenia, rheumatism, or gout, together with some exciting cause. Neuralgic pain not infrequently follows pressure, bruising, or injury of the brachial plexus, in whole or in part, and is of course one of the prominent symptoms in neuritis. Sometimes the cause is one acting reflexly, as for example heart or aortic disease producing angina pectoris, or an aortic or subclavian aneurysm. Diseases causing toxic neuritis, such as rheumatism, gout, diphtheria, enteric fever, and influenza, may certainly cause brachial neuralgic pain; and peripheral injuries to nerves may produce ascending neuritis, accompanied by agonising pain. But in persons predisposed to neuralgia the immediate cause may be of the same nature as that in the craft-palsies. Pianists, violinists, telegraphists, and clerks, suffering from such palsy, generally complain also of neuralgic pain; and certainly in such cases the general health is often, if not always, below par. There is a special form of trade neuralgia affecting the arm from the external condyle of the humerus and the region of the head of the radius down to the fingers. It is the result of strain or excessive use of certain muscles. Similar neuralgic pain is produced by over-indulgence in tennis (Clado and others). Redness and swelling occur in these cases, and probably a considerable amount of the pain may be rightly referred to the muscles as well as to the nerves. There still remains a well-defined group of cases due to hysteria or neurasthenia, which may present considerable difficulty before the true nature of the case is recognised.

*Symptoms.*—The pain is of the usual neuralgic nature, dull and boring, with lancinating paroxysms more or less severe. The affected nerves are tender on pressure; and there are certain painful points in the axilla, over the circumflex nerve near the deltoid muscle, over the radial nerve where it turns round the humerus, over the ulnar nerve posteriorly and the median anteriorly at the elbow-joint, and at other points in the lower arm. There may be hyperaesthesia, anaesthesia or paraesthesia, herpetic eruptions, vasomotor disturbances such as hyperidrosis and muscular atrophy especially when neuritis is present. In a true neuritis, pressure on the affected nerve induces pins-and-needles sensation. As a rule the pain is greatly increased on movement; and the limb is to be kept at rest as far as possible. If the pain be limited to a particular area the ulnar is the nerve which suffers most frequently (Heinlain).

The *diagnosis* is easy; it is more important to discover the cause of the condition with a view to successful treatment.



The *prognosis* in simple neuralgias is usually favourable ; but here again the causation is of the utmost moment.

The *treatment* is that generally used for neuralgia ; namely, rest, local sedatives or counter-irritants, together with active treatment of the etiological factors.

**Brachial Neuritis.**—The nerve-roots may be affected especially in spinal disease, or where growths involve the nerves at or near their exit from the spinal canal ; and to this form the name of radicular brachial neuritis is given. When the nerve-roots or the brachial plexus itself are affected the condition is generally a perineuritis (Oppenheim).

*Etiology.*—The radicular form, as indicated above, depends on injury from spinal or possibly from meningeal disease. Brachial neuritis proper is rare ; it is due to the ordinary causes of neuritis elsewhere, and is perhaps especially associated with gout or rheumatism. It occurs more frequently in women, and generally after middle life (Prinee).

The *clinical history* is generally characteristic of a perineuritis. Pain is a constant phenomenon ; slight at first and often referred to a distant part of the limb, such as the hand, back of the forearm, or near the axilla, or in the region of the scapula, it soon becomes more severe and more definitely associated with the plexus and the nerves arising from it. At first the pain may recur at considerable intervals, but later it becomes continuous, and generally there are paroxysms of an acute lancinating kind. It is increased on movement, and is frequently, during the paroxysms at least, somewhat diffused ; if on the left side, it may closely suggest the pain of angina pectoris, the resemblance being rendered greater by irregular cardiac action or palpitation. There is often hyperaesthesia or hyperalgesia of the affected area, and there may be temporary anaesthesia. There may be loss of muscular power in the hand or arm, with atrophy of the affected muscles, but this is generally a late phenomenon, and is usually slight in degree. The trophic changes, in severe or long-standing cases, are frequently well marked—such as “glossy skin” (*vide* p. 82), local subcutaneous oedema, wasting of muscles, and changes in the affected joints.

In radicular neuritis the pain felt near the spinal column, referable to the posterior cutaneous branches, and the presence, sometimes demonstrable by other phenomena, of bone disease or other cause of the condition, are usually sufficient, sooner or later, to clear up the nature of the case.

*Diagnosis.*—Neuralgia is simply nerve pain ; but it is generally easy to decide whether there is or is not neuritis by attending to two points, namely, the presence or absence of marked or persistent tenderness along the line of the nerves, and whether movement of the affected arm is painful or not. Neuritis is always accompanied by these features, and the appearance of trophic changes in muscle and skin renders the diagnosis more certain.

In angina pectoris the pain shooting down the arm is not accompanied by so much tenderness on pressure over the nerves, and cardio-arterial disease is usually present.

Rheumatoid arthritis, with its peculiar joint-changes, has a distinctive history, and there is no nerve tenderness.

The *prognosis* depends almost entirely on the severity of the neuritis, and the consequent interference with the integrity of nerve-fibres. Once the skin becomes glossy, the muscles atrophied, and joints more or less fixed, a complete cure is very problematical; and the patient finds that the affected limb is not merely almost useless, but the source of continual trouble. On excessive attempts at using the limb there is generally considerable pain, much like rheumatism, increased by cold weather; and formication, tingling, or burning, sometimes accompanied by muscular spasms, are frequently induced by the same causes.

Neuritis is always tedious, and more so if severe; and in all cases in which vitality is much below par the prognosis must be guarded. In some cases relapses occur, but such relapses are frequently due to carelessness on the part of the patient, or too vigorous treatment on the part of the medical man.

The *treatment* differs in no way from that of neuritis elsewhere. Rest is of the greatest importance, and should be as complete as possible, with the arm not merely in a sling, but bandaged to the chest, so as absolutely to prevent all movement. For the acute stage, poultices, hot fomentations, and, if necessary, morphine or cocaine hypodermically should be used. After the inflammation has subsided massage and passive movements may be carried out, but with the greatest care. Hot water is of benefit in combating contracture, and galvanism is sometimes efficacious, although more as a sedative than a restorative.

**Paralysis of the Brachial Plexus.**—The plexus, or the nerve-roots forming it, may be injured in many different ways. Sometimes the whole of the plexus is affected, frequently, however, a part only. Tumours or spinal disease may affect the nerve-roots (Apert); and injuries in the neighbourhood of the plexus, such as dislocation of the humerus, or fracture of the head of the humerus or scapula, may cause a more or less complete paralysis of nerves arising from it. Brachial neuritis may cause paralysis (*vide* p. 389); and in ascending neuritis, an injury to one nerve may set up inflammation, which may spread to the whole of the brachial plexus.

I. *The whole Plexus may be affected and all the Nerves paralysed.*—These cases are almost always traumatic in origin; and the commonest causes are subluxation of the humerus, fractures in the region of the axilla, and injury during parturition (Weil); very frequently the paralysis becomes more and more limited, until only one or two nerves remain affected—often the circumflex and musculo-spiral (Ballet, Dejerine).

The clinical history varies greatly, beginning with a general weakness and heaviness of the limb, and going on perhaps to paralysis of motion and sensation, with wasting of muscles and trophic changes in the skin or joints; but very frequently the disease becomes limited in time to one or more nerves.

The diagnosis is generally comparatively easy; and the prognosis

depends greatly on the extent and nature of the injury, the electrical reactions, and the more or less rapid recovery of the functions of the affected nerves.

II. *Erb's Paralysis, or the Upper-Arm Type of Paralysis*.—This is due to a lesion of the fifth and sixth cervical roots. The muscles affected are the deltoid, biceps, brachialis anticus, supinator longus, sometimes the supinator brevis, supraspinatus, and infraspinatus. The cutaneous supply from the two affected roots goes to the area of skin controlled by the circumflex and musculo-cutaneous nerves, including the outer side of the upper and lower arm.

Etiology.—Injuries generally produce this form of paralysis. Not infrequently it is caused by pressure above the clavicle close to the side of the neck; thus masons' labourers and porters supply many of the instances of this somewhat rare type of paralysis. Operations in the supraclavicular fossa and tumours of the cervical vertebrae may also cause this paralysis. Dr. F. Buzzard has called attention to cases of uniradicular palsy of the brachial plexus in which *one* spinal nerve suffers. The motor palsy is more complete than the sensory, and he believes the lesions to be vascular in nature.

When the arm is raised above the shoulder and carried backwards, or when from the weight carried the head is twisted round backwards to the same, or to the opposite side, the fifth and sixth cervical nerves are more liable to be compressed. In infants, traction on the neck at birth may cause Erb's paralysis (Babonneix and Voisin); and, lastly, in a few isolated cases the lesion was apparently of toxic origin.

Symptoms.—The arm cannot be abducted, and, as the anterior part of the deltoid may obtain some of its supply from the anterior thoracic nerves, it can in these cases only be feebly carried forward. The arm cannot be flexed at the elbow, and supination is impossible, especially when the supinator brevis is affected. The arm is also turned somewhat inwards, and the humerus cannot be rotated outwards. Generally in cases occurring in adult life the affected muscles waste; the reaction of degeneration is obtainable, often complete, sometimes only partial; and the paralysis is severe and of long standing. The sensory changes vary greatly. There is often pain, and there may be anaesthesia in the sensory realms of the circumflex and musculo-cutaneous nerves, or in one alone (Weber).

The *diagnosis* does not present any difficulty, unless, as sometimes happens, the paralysis is not limited to the fifth and sixth cervical nerves.

The *prognosis* should be given with care; the cases are usually tedious, and the paralysis may persist without improvement.

III. *The Lower-Arm Type of Paralysis*.—One form of this is *Dejerine-Klumpke's paralysis*, in which the eighth cervical and first dorsal roots are affected. The muscles chiefly affected are the small muscles of the hand (the muscles of the ball of the thumb, of the little finger, and the interossei), and the flexors of the fingers in the forearm (Heubner).

In other cases the seventh and the sixth cervical roots suffer also, and



involve paralysis of the extensors of the fingers, the triceps, pronators and flexors of the wrist.

Traction on the arm tearing the nerve-roots, tumours or caries of the vertebrae, tumours pressing on the nerve-roots, the existence of a seventh cervical rib (Thorburn, H. L. Jones), syphilitic meningitis, and primary neuritis of the nerve-roots are among the assigned causes of this condition.

The affected muscles waste, and the paralysis depends on the extent of the lesion. Pain, hyperaesthesia, and anaesthesia are more marked in the ulnar region of the forearm and upper arm, and sometimes in the area controlled by the median nerve. Not infrequently there are marked ocular phenomena, dependent on the injury of communicating sympathetic root branches of the first dorsal root. These include myosis on the side of the lesion, sluggish contraction of the pupil, and diminution in size of the palpebral fissure with retraction of the eyeball.

The *prognosis* varies; recovery may occur in two or three months, or, where the nerve-roots are permanently damaged or torn, operative interference may afford the only chance of cure.

**Paralysis of the Long Thoracic Nerve, or Nerve to the Serratus Magnus.**—This nerve is formed in the scalenus medius muscle by branches from the fifth and sixth cervical nerves. It runs a long course, passing behind the brachial plexus, and enters the muscle at its lower border.

*Etiology.*—The nerve may be injured by pressure or by a punctured wound. The carrying of heavy weights on the shoulders, especially if a sharp edge press heavily into the neck, or constant muscular contraction of the scalenus medius through which the nerve passes, may set up neuritis in the nerve. The condition is therefore much commoner in men and on the right side. Muscular contraction of the scalenus medius is almost continuous in trades in which the worker has his arm continually raised, as in plastering ceilings (Fraser, K tli).

Isolated invasion of this nerve by toxic neuritis has been found after diphtheria, enteric, and influenza, although very rarely; cold air blowing on the neck is a possible cause. In progressive muscular atrophy the serratus muscle is often affected.

*Clinical History.*—The serratus magnus muscle carries the scapula outwards, forwards, and slightly upwards. It fixes the scapula when the arm is raised above the horizontal. When the arm is raised vertically, and the scapula fixed by the rhomboids, etc., it can raise the ribs, and by expanding the chest in this way greatly helps forced inspiration.

When the serratus is paralysed the scapula is nearer to the spinal column, is higher in position, and is not kept in close apposition to the chest. When the arm is brought forwards the scapula rotates vertically, the posterior border projecting like a wing, and the lower angle being rotated backwards towards the spinal column, and also upwards. In most persons with this paralysis the arm cannot be extended beyond the horizontal, unless the scapula be fixed artificially; although in some



individuals—according to Jolly, Bruns, and others—the lower and middle fibres of the trapezius, the supra- and infra-spinatus, and the posterior part of the deltoid can act in this way. Forced inspiration is interfered with, and when the arms are raised vertically the deficient expansion of the chest on the affected side becomes obvious. The ability for physical work of the patient is much interfered with by the fact that when the arm is raised he cannot push forwards with the affected arm. There is generally more or less pain before paralysis becomes marked; and the electrical reactions help to clear up the condition. The *diagnosis* presents no difficulty. The *prognosis* is favourable in toxic cases; but where the nerve has been injured by pressure, recovery is generally tedious. The electrical reactions are often of great prognostic value.

*Treatment.*—Rest is secured for the affected limb, care being taken to prevent contractions of the scalenus medius. This is best carried out by keeping the arm in a sling, and forbidding any attempt at raising the shoulder. Faradism, when the neuritis has subsided, may be of use to keep up the nutrition of the muscle, and the galvanic current has been sometimes found of value, the kathode in the supraclavicular fossa and the anode over the nape of the neck.

**Paralysis of the Suprascapular Nerve.**—This nerve arises from the trunk formed by the union of the fifth and sixth cervical nerves, and a branch of the fourth. It may be damaged alone, or with the circumflex nerve. Dislocation of the humerus, falls on the shoulder or on the hand causing contusion of the shoulder-joint, the carrying of heavy weights, and a toxic neuritis (P. Ewald), cause this somewhat rare paralysis (Dorrien).

The nerve supplies the supra- and infra-spinatus muscles. The supraspinatus, according to Duchenne, not merely helps to raise and also to bring forward the arm at the shoulder-joint, but it also keeps the head of the humerus in close apposition to the glenoid cavity. Hence in cases of paralysis of this muscle there is difficulty in raising the arm, and also a tendency to subluxation of the head of the bone when the deltoid lifts the arm. The infraspinatus rotates the humerus outwards, although it does not act unassisted, as the posterior part of the deltoid and the teres minor act in this way, and these muscles tend to become hypertrophied when the infraspinatus is unable to undertake its share of the work. Hence writing, sewing, and any movements of outward rotation of the arm become difficult. The affected muscles waste, and the absence of the infraspinatus is readily distinguishable.

There may be some anaesthesia over the scapula, and a certain amount of pain on movement is not uncommon.

**Paralysis of the Nervus Dorsalis Scapulae.**—This nerve supplies the levator anguli scapulae and the rhomboids, and sends a few small branches to the serratus posticus superior. Its paralysis is very rare, but may result from neuritis or from injury. The levator anguli raises the scapula, while the rhomboids draw the shoulder-blade upwards and very markedly backwards so as to approximate it to the spinal column. These

movements are interfered with in paralysis of this nerve, and there is a loss of fixation of the scapula greatly limiting the usefulness of the arm.

**Paralysis of the Circumflex Nerve.**—This nerve is derived from the posterior cord of the brachial plexus, and supplies the deltoid muscle (with the exception of a small anterior part which occasionally receives a small branch from one of the anterior thoracic nerves), the teres minor, and the skin over the region of the deltoid.

*Etiology.*—The course of the nerve renders it especially exposed to damage; therefore, in injuries to the shoulder, it may suffer as in falls and dislocations, and sometimes it is pressed upon by the head of a crutch. Neuritis may occur in this nerve, and it has been noted in cases of lead poisoning, fevers such as enteric and influenza, and in diabetes (Disen).

*Clinical History.*—The deltoid is paralysed, and the arm cannot be raised, except by the comparatively feeble supraspinatus and, occasionally, by the anterior part of the deltoid. The deltoid wastes and the shoulder-joint often becomes stiff from adhesions, because the nerve appears to supply some trophic branches to the joint. The teres minor paralysis is not apparent. There is often pain and sometimes anaesthesia over the upper and posterior third of the upper arm, but this may be absent.

*Diagnosis.*—Care must be taken in diagnosing ankylosis of the shoulder-joint, such as occurs in cases of rheumatoid arthritis, from paralysis of the circumflex. In ankylosis the scapula follows the head of the humerus when the arm is moved, and the deltoid can be made to contract, although it may be unable to produce any effect; the absence of anaesthesia is also important in diagnosis. An electrical examination should not be neglected.

*Treatment.*—Besides adopting the usual measures suitable for treating neuritis of any nerve and for preserving the nutrition of the deltoid, much may be done by educating other muscles to take up the duties of the deltoid, especially when the deltoid is permanently paralysed.

**Paralysis of the Musculo-Cutaneous Nerve.**—The musculo-cutaneous is derived from the fifth and sixth cervical nerves, and supplies the chief flexors of the elbow and the skin over the radial side of the forearm. The nerve is rarely affected alone, more commonly it suffers with the brachial plexus; injuries of different kinds in the region of the shoulder have caused the recorded cases.

The biceps and brachialis anticus can no longer flex the arm at the elbow; and, when the hand is supinated, the supinator longus is unable to act as a flexor. The muscles waste, and there is generally anaesthesia over the radial side of the forearm, both anteriorly and posteriorly, down to the ball of the thumb and the palm of the hand.

The nerve to the coraco-brachialis muscle, which is closely related to the trunk of the musculo-cutaneous, may escape. In Erb's juvenile type of dystrophy there is atrophy of the flexors of the forearm, but there is no history of injury, and the condition has lasted for years and probably since childhood (*vide* p. 41).

**Paralysis of the Musculo-Spiral Nerve.**—The musculo-spiral nerve is derived from all the roots making up the brachial plexus, except the first dorsal. It supplies the following muscles: the triceps, the anconeus, the extensor carpi radialis longior, the extensor carpi ulnaris, the extensor communis digitorum, the three extensors of the thumb, the special extensors of the index finger and little finger, and the two supinators. The cutaneous supply includes the radial side of the forearm and hand, and a part of the upper arm.

*Etiology.*—The course of the nerve and its exposed position render it very liable to injury by pressure; and in 242 cases of paralysis of the arm, collected by Remak, 105 were due to a lesion of this nerve. It should also be remembered that in topers and cachectic persons, pressure which would be trivial in the robust may cause paralysis. A misfitting crutch may press on the musculo-spiral; and the "Saturday night paralysis," brought on by falling asleep with the arm over the back of a chair, is generally due to a lesion of this nerve. Sometimes sleeping on the arm when in bed causes it, especially if the bed be unusually hard. The continental device of tying prisoners' hands together behind their backs frequently produces this paralysis; and the Russian custom of tying infants' arms to their sides has occasionally caused it. Fracture of the humerus may also cause paralysis (Chanoz, Lehmann).

Toxic agents may produce an isolated lesion of this nerve, but generally the site of the lesion is determined by a local injury of some kind. Lead, arsenic, and silver may bring about this paralysis, but here again the cause is generally toxico-traumatic. Rarely, violent muscular contractions of the triceps, especially of the outer head, have produced paralysis (Gerulanos); and lastly, hypodermic injections of ether, chloroform, or other drugs, in the vicinity of the nerve, not necessarily into its substance, are responsible for a small number of cases (Potain).

*Clinical History.*—Not infrequently the triceps or the supinator longus escapes, especially if the site of the lesion be near the middle of the humerus. In most cases there is paralysis of the extensors of the elbow and wrist, and of the long extensors of the fingers, giving rise to a very typical wrist-drop, the fingers being bent at the metacarpo-phalangeal joints, and the thumb somewhat apposed and sunk. In long-standing cases the flexors, not being properly opposed, lose their power, and the pronators become shortened. Sir W. Gowers points out that in some cases there is a gradation of extensor paralysis in the fingers, being most marked in the fourth finger and less marked towards the first. Not infrequently there is some tingling or even anaesthesia; but in cases due to pressure sensory phenomena are usually slight. The affected muscles waste, and the sheaths of the tendons may swell, and sometimes the joints.

*Diagnosis.*—It is generally easy to distinguish this condition from lead paralysis, because, first, only one arm is affected; secondly, the supinator longus muscle is usually affected, whereas it generally escapes in saturnine paralysis; and thirdly, the onset is sudden.



*Prognosis.*—Pressure paralysis for the most part is rapidly recovered from; but for determining the probable duration of the condition no test is so satisfactory as the electrical reactions.

The *treatment* is on general principles; the utmost care being taken to prevent pressure on the nerve, and, where neuritis has been set up, to give rest to the affected limb.

**Paralysis of the Median Nerve.**—The nerve is derived from the lower three cervical and the first dorsal nerves, and arises from two roots, one from the outer and the other from the inner cord of the brachial plexus. It supplies the two pronators, the flexors of the wrist (except the flexor carpi ulnaris) and of the fingers (except the ulnar half of the deep flexor), the opponens, the two flexors, and the short abductor of the thumb, and the radial lumbricals. Its cutaneous supply includes the radial side of the palm, the front of the first, second, and half of the third fingers, and sometimes the back of the last phalanges of the thumb and first three fingers.

*Etiology.*—The nerve is generally injured in the forearm by fractures of the radius or ulna, or by wounds just above the wrist. Esmarch's bandage is responsible for a few cases; and in some occupations, such as cigar-making (Coester) and carpet-beating (Reinhardt), paralysis of the median nerve has been recorded. Powerful contraction of the pronator radii teres may also cause the condition (Bernhardt).

*Clinical History.*—If the injury include all the muscular branches pronation is impossible, and the patient endeavours by rotating the upper arm inwards to compensate for the paralysed muscles. The wrist cannot be flexed except towards the ulnar side; the thumb is constantly extended and abducted, and cannot be apposed to the tips of the fingers. The fingers cannot be properly bent at the first interphalangeal joint, and only the last three fingers can be bent at the second. The interossei can flex the first phalanx; and their unopposed extensor action on the second and terminal phalanges causes a tendency to subluxation. Where the lesion is sufficiently low down, the smaller muscles of the hand may suffer alone.

Not infrequently the lesion is severe and the thenar muscles waste. Sensory changes are common; pain and tingling may be present, or anaesthesia more marked, as a rule, on the palmar surface. The affected skin is often cold and cyanosed, and herpes or even bullae resembling pemphigus may appear. In some cases the nails become brittle or furrowed, or may fall off (K. Hirsch).

*Diagnosis* is easy. In *prognosis* the electrical reactions are important. The *treatment* is on the usual lines.

**Paralysis of the Ulnar Nerve.**—The ulnar arises from the last cervical and first dorsal roots, and is associated with the lowest part of the cervical enlargement of the cord. It supplies the flexor carpi ulnaris, the ulnar half of the deep flexor of the fingers, the muscles of the little finger, the palmaris brevis, the interossei, the inner two lumbricals, and the adductors of the thumb. The cutaneous supply is confined to the



ulnar side of the hand, and, according to most authorities, to the back of two and a half fingers, and the front of one and a half.

*Etiology.*—This nerve is more commonly affected than the median, and may suffer along with it. When the injury is in the upper arm, one of the commonest sites of lesion is at the elbow-joint, where fracture of the internal condyle of the humerus, or a supracondylar fracture may readily implicate the nerve. In some instances, months after such a fracture, the nerve may be pressed upon by callus (Destot). Dislocation of the shoulder or elbow, wounds at the elbow-joint or in the forearm may all cause it. Duchenne directed attention to occupation-paralysis of this nerve. It may occur where, in working, pressure is continuously exerted on the elbow. The nerve is also apt to suffer from prolonged flexion of the arm at the elbow-joint, especially in feeble or cachectic persons, or in those liable to neuritis from alcoholism, lead poisoning, or other cause. Hence it is a common form of sleep paralysis, and in not a few cases in which there is predisposition, even bending of the elbow causes numbness or tingling along the line of the nerve. A neuritis may readily be set up in these cases (Sherren).

*Clinical History.*—On flexion the wrist is bent towards the radial side: the fingers cannot be flexed at the first or extended at the second joints, and this is especially the case with the last two fingers. The interossei are paralysed, producing eventually the claw-like hand or “*main en griffe*”; although it should be stated that the first two fingers are not claw-like, because the two radial lumbricals are not paralysed. The fingers cannot be separated or adducted; the thumb sticks out prominently, and may be slightly rotated forwards. The muscles affected may waste, and the hypothenar eminence disappears. The sensory changes are often severe, pain and tingling being common; not infrequently the presence or absence of anaesthesia is out of all proportion to the gravity of the lesion.

The *diagnosis* rarely presents any difficulty, the claw-like hand differing, as mentioned above, from that found in progressive muscular atrophy.

The *prognosis* is generally favourable, though a period from a few weeks to months may elapse before complete recovery; or an operation, such as removal of callus, may be requisite before the nerve can resume its normal functions.

#### Neuralgia of the Lumbar Plexus, or Lumbo-Abdominal Neuralgia.

—As in intercostal neuralgia, so the nerves of the lower part of the trunk may be affected, and may give rise to lumbo-abdominal neuralgia.

There are certain painful points, often tender on pressure, and among these the most important are: an *iliac* point near the iliac crest; a *hypogastric*, over the lower part of the rectus abdominis muscle; a *scrotal* point in males, and a *labial* point in females. Sometimes pain shoots along the spermatic cord, and it is quite probable that irritable testicle is, in many cases, of neuralgic origin.

The *causes* are those productive of neuralgia elsewhere. First, of

a general kind, such as prolonged ill-health, anaemia, or neurasthenia; and, secondly, some proximate cause capable of producing neuralgia in those rendered susceptible, and generally accounting for the selection of a certain nerve or nerves.

The local causes are pelvic disease—constipation very frequently, uric acid causing pain in the penis, and analogous agents. There is not infrequently cutaneous hyperaesthesia, and sometimes herpetic eruptions appear along the line of the affected nerves. Occasionally, although rarely, it causes sexual excitement, seminal emissions, and increased frequency or pain in the act of micturition.

Crural neuralgia may follow a lesion of the lumbar plexus, or it may be secondary to sciatic neuritis. The cutaneous branches of the anterior crural nerve are perhaps more frequently affected. Herpes and hyperidrosis are not uncommon. There may be neuralgic pain in the line of the obturator nerve, but it is rare.

The *diagnosis* of these neuralgias is not difficult, especially where the cause of the condition is apparent. Tumours or other pathological conditions of the pelvic organs should be sought for; and special care should be taken to investigate the condition of the generative organs, the bladder, and the rectum.

The *prognosis* depends on the cause; an idiopathic neuralgia is of no great importance; where anaesthesia or paraesthesia is well marked, there is much more probability that an organic lesion is present, and therefore a more guarded prognosis should be given.

The *treatment* must be conducted on general principles.

**Paralysis of the Lumbar Plexus.**—The lumbar plexus arising from the first three lumbar roots and half of the fourth, with a connecting link from the twelfth dorsal root, is formed in the substance of the psoas muscle, and supplies the flexors and adductors of the thigh, the extensors of the knee, and the cremaster muscle. It supplies also the skin over the lower part of the abdomen, the scrotum and root of the penis or labia, the anterior and both internal and external surfaces of the thigh, and the inner surface of the leg and foot.

The lumbar plexus may be damaged in whole or in part by—(i.) Disease of the spinal column, such as caries or tumour; (ii.) Tumours of the meninges, or inflammatory or other exudations; (iii.) Disease of the cord; (iv.) Invasion of the roots, loops, or cords forming the plexus, by tuberculous or other affection of the retroperitoneal glands, by psoas abscess, rarely by a primary neuritis, or a neuritis secondary to disease of the sacral plexus.

More commonly the following component nerves of the plexus suffer:—

**Paralysis of the Obturator Nerve.**—The obturator and accessory obturator nerves supply the three adductor muscles of the thigh—the gracilis, the obturator externus, and in some cases the pectineus. The cutaneous distribution is confined to the inner side of the thigh, and to the inner and upper part of the leg.

This nerve may be injured by pressure during parturition, more commonly by pelvic tumours or obturator hernia. Paralysis of this nerve implies loss of power in the adductors of the thigh, inability to cross the legs, difficulty in both inward and outward rotation of the leg, and anaesthesia over the upper third of the inner surface of the thigh, sometimes extending nearly as low as the knee. Both walking and horse-riding are fatiguing, and the patient cannot grip the saddle with his knees.

**Paralysis of the Anterior Crural Nerve.**—This nerve supplies all the muscles on the front of the thigh, and also the iliacus and pectineus. The cutaneous distribution includes the front and inner side of the thigh below the domain of the ilio-inguinal and genito-crural nerves, and also the inner side of the leg and foot down to the great toe. This nerve may be injured in many ways—by spinal caries or tumour, by psoas abscess, by dislocation of the hip-joint, not infrequently by wounds in the groin or thigh, and rarely during parturition. In disease involving the roots, the nerve may appear to be specially affected. The nerve itself is most commonly injured in the groin or thigh. When damage is sustained within the pelvis, the branch to the iliacus may be involved, and then flexion of the hip becomes difficult. Bruns records a case of diabetes mellitus in which the anterior crural nerve alone was affected; neuritis of this nerve may appear after enteric fever or diphtheria as well as in chronic alcoholism (Gumpertz). Lastly, in anterior poliomyelitis the muscles supplied by this nerve may suffer chiefly or solely.

When the lesion is complete, the motor paralysis is serious because the flexors of the thigh at the hip-joint and the extensors of the knee are supplied by this nerve, and these muscles waste. The knee-jerk is abolished, and the paralysed leg is dragged along, the patient being in danger of falling should the knee suddenly flex. The anaesthetic area includes the inner side and front of the thigh, the inner side of the leg down to the toe, including the great toe, and the adjacent side of the second. Pain in the line of distribution of the nerve is common, especially when the lesion is near the spinal column and when the condition is in the irritative stage. Very commonly the anterior crural nerve is affected in part only, the motor and sensory phenomena being correspondingly limited.

The *treatment* of many cases of crural paralysis is surgical. In other cases faradism and galvanism may be of value. Where there is permanent paralysis, as in cases of poliomyelitis, transplantation of tendons has proved of very great benefit. F. Krause has transplanted the flexors of the leg into the anterior surface of the thigh, and so compensated for the muscular atrophy.

**Paralysis of the Superior Gluteal Nerve.**—This nerve belongs to both the lumbar and sacral plexuses, and it supplies the gluteus medius and minimus. It is rarely affected alone, and when it is, there is inability to abduct and circumduct the thigh.

**Neuritis of the External Cutaneous Nerve.**—This nerve arises from



the second and third lumbar nerves, and supplies the outer surface of the thigh from the hip-joint nearly to the knee. A special form of neuritis of the nerve has been described by Bernhardt (1895), and named by Roth *meralgia paraesthetica*; in 1900 Musser collected 89 cases; it has been thought to be due to pressure exerted by the fascia on the nerve, but it is generally of alcoholic origin, and is not confined to this nerve alone. Besides pains along the lines of distribution, there is sometimes difficulty in standing and walking, probably due to the loss of some controlling influence of the nerve over the fascia.

**Sciatica.**—This most indefinite name is applied to three conditions producing pain in the sciatic nerve: (1) a true neuralgia of the nerve or its branches; (2) pain produced by pressure on the nerve by a tumour in the pelvis, by inflammation of the hip-joint or other cause; this group may be called pressure-sciatica; (3) sciatic neuritis which constitutes the ordinary form. This is generally an interstitial neuritis or perineuritis, and only rarely, as in alcoholic or other similar forms of toxic neuritis, is it parenchymatous. Lesions of the nerve-roots, of the cauda equina, and even of the spinal cord may also cause sciatic pain, but in these conditions it is generally bilateral.

It is difficult to assert that pure neuralgia of the sciatic nerve cannot or does not occur. Neuralgia may be the expression of nerve exhaustion, and therefore after excessive use of the legs there is no reason why a sciatic neuralgia should not occur. But it is rarely seen in such circumstances, because both sciatic nerves are rarely affected at the same time. Still, just as a carious tooth may set up a trigeminal neuralgia, so the sciatic pain felt in hip-disease may be a true secondary sciatica, really neuralgic, and not due to pressure or direct inflammatory implication. Small branches pass to the posterior aspect of the hip-joint from the sacral plexus and the great sciatic nerve; this has an important bearing. Neuralgia of the sciatic nerve when it does occur is generally easily traced to some definite cause. Pressure-sciatica, if not neuralgic, is due to pressure or direct contact with an inflammatory focus. The pain is not increased by digital pressure on the nerve unless the cause of the pressure has also set up an inflammatory neuritis.

Whilst these three forms must all be borne in mind in describing sciatica, sciatic neuritis is the most common, and therefore most important form.

**Etiology.**—Sciatic neuritis is much more frequent in men than in women, the proportion varying from two to four times as many, the latter estimate being more nearly correct. It is most common between the ages of forty and fifty, less frequent between fifty and sixty, much less frequent between thirty and forty, and rare in the earlier and later decades of life. Rheumatism and gout are the principal disposing, cold and wet the chief exciting, causes. Heavy muscular exertion has been found to be a cause, especially in gouty or rheumatic subjects. Occasionally after a severe attack of lumbago the sciatic nerve has become involved in a rheumatic perineuritis. Certainly in persons so disposed, pressure on a



hard seat, or, as Sir W. Gowers states, exposure in a cold draughty water-closet may bring on an attack. Syphilis is not a common cause, and generally in specific cases with sciatic pain there is a primary spinal meningitis or a cord lesion. It is possible that in rare instances a severe muscular contraction might set up a sciatic neuritis, but some pre-existing cause should be sought for. Pressure-sciatica is often associated with pressure of the fetal head in the later months of pregnancy. It is also commonly due to a loaded rectum; pelvic tumours, pelvic inflammation, exostoses, and so forth may also exert pressure on the nerve.

Neuralgia, as stated already, is due to an irritant acting reflexly, the remoter causes, if any, being anaemia or malnutrition of the nervous system generally. Joint disease—tuberculous or osteo-arthritis,—tuberculous or other lesions of the vertebrae or of the sacro-iliae synchondrosis, and similar conditions may cause neuralgia of the sciatic nerve, or may, in addition, lead to a true neuritis of the nerve. Lastly, blows or injuries of many kinds may set up a true neuritis or perineuritis, a pressure or secondary sciatica, or a pure neuralgia.

Our knowledge of the *morbid anatomy* of sciatic neuritis is derived from the appearance and microscopical examination of the nerve in cases in which stretching or removal of portions of the nerve has been performed. The nerve is seen to be reddened and swollen, and there is marked exudation into the sheath, and especially into the connective tissue between the funiculi. Haemorrhages have often been found. Where the endoneurium (connective tissue inside the funiculi) is involved, the nerve-fibres are very apt to undergo degeneration. These changes may extend along the greater part of the nerve-trunk, but are most marked in two positions—at the sciatic notch and in the middle of the thigh. In pressure-sciatica long-continued pressure may mean Wallerian degeneration of the nerve-fibres with consequent atrophy of the muscles. In neuralgia anatomical changes do not necessarily occur.

*Symptoms and Signs.*—The great symptom is pain, whether the case is one of sciatic neuralgia, pressure on the sciatic nerve, or sciatic neuritis. It may come on gradually, tending to increase in violence and to get worse on muscular effort, on pressure over the nerve-trunk, and often towards night; or the pain may come on suddenly, and may or may not be paroxysmal in character. Where it comes on gradually, only certain movements which cause pressure on the nerve are painful, but eventually even the slightest movement may be accompanied by pain. Walking may only be possible with the knee bent. The pain is often burning or gnawing, and may be constant or may increase at times in severity. Certain painful parts may be indicated by the sufferer, the two commonest being the sciatic notch and the middle of the thigh. Not infrequently the pain, limited at first to the upper part of the thigh, spreads downwards to the heel. Pain is also specially referred to the following regions: above the hip-joint, the popliteal space, below the head of the fibula, just behind the external malleolus, and the dorsum of the foot. In protracted cases groups of muscles may waste, and if so, cramps and

even fibrillar twitchings often appear in them. Among the muscles so affected are the hamstrings, the calf muscles, the tibialis anticus and peroneal muscles, and the glutens maximus. It is not very uncommon in severe cases to hear the patient complain of numbness, tingling, and formication, and sometimes there are areas of complete anaesthesia, although it is more usual to find areas of partial anaesthesia and analgesia on the back of the leg or thigh. These sensory phenomena imply a marked interference with nerve-conduction; in other words, a severe interstitial inflammation in the nerve. Where the skin on the back of the thigh is anaesthetic, the small sciatic nerve is involved also. Sometimes herpetic eruptions occur, and occasionally oedema of the affected leg may be present. As a rule, however, vasomotor and trophic phenomena are not prominent. In pure neuralgic cases the pain comes on periodically. It may be aching with occasional paroxysms, or it may be distinctively paroxysmal in type. There is no alteration of cutaneous sensibility. Dr. Crawford Renton considers that perineuritis, which he believes tends to cause adhesions, shews its presence when the patient tries to walk. It comes on after some minutes of exercise, and it ceases when the patient lies in bed or remains quietly standing. In a considerable number of cases, interstitial neuritis is wider in its attack than the perineurium, and when the endoneurium in the funiculi is invaded, there is much and often continuous pain with little respite. In parenchymatous neuritis there is severe pain with pronounced sensory changes and wasting of the affected muscles, but as a rule it is symmetrical, and other nerves besides the sciatic suffer.

In pressure-neuritis, although there is pain radiating along the nerves from the site of the pressure, there is, as a rule, no increase of tenderness on palpation of the nerve.

The *diagnosis* is generally made by digital examination over the nerve. In sciatic neuritis pressure on the nerve, or putting the nerve on the stretch, is sufficient to cause pain. It is easy to effect this either by exercising deep pressure on the nerve in the buttock or in the middle of the thigh, or else by flexing the leg at the hip-joint and exerting pressure in the popliteal space.

Pressure-sciatica can generally be diagnosed by investigating the pelvic contents by rectal or vaginal examination, when the underlying cause may be revealed; or, as mentioned above, by exerting pressure upon the nerve when little if any additional pain is experienced.

In disease of the sacro-iliac synchondrosis pain may radiate widely, but not usually so far as even the upper part of the thigh. Hip-joint disease may cause a secondary sciatica, probably neuralgic; if it does not, the pain is at any rate circumscribed, and the position of the limb, although to some extent resembling the semi-flexed limb of a sufferer from severe sciatica, is characteristic.

In lesions of the cauda equina or nerve-roots, whether by tumour or inflammation, the symptoms are generally bilateral, and not, as in sciatica, limited to one side.

In tabes the lightning pains are generally bilateral ; and the ataxic and other characteristic phenomena amply suffice for diagnosis.

*Prognosis.*—Sciatica is apt to be obstinate, and may last for months or even years, with a certain amount of remission as regards degree of pain. Sciatica may even keep the sufferer completely confined to bed, but in these cases the sciatic neuritis is extremely severe and protracted. Muscular atrophy, with cramps and fibrillar tremors and anaesthesia over a wide area, indicate a considerable degree of interstitial neuritis, and a definite, if not necessarily permanent, lesion of the nerve-fibres themselves. The prognosis of most cases of sciatica is, however, favourable and the treatment successful ; but the probable duration of the attack, even with active treatment, should be estimated in a guarded manner.

In *treatment*, attention should always be directed at once to the possibility, or rather probability, of a constitutional element in the case ; and rheumatism should be assailed with salol, salicylate of sodium, or aspirin, gout with colchicum, salines, and dietetic measures. If there be a distinct history of rheumatism, however slight, salicylates and a saline purge should invariably be administered at once.

Locally, in mild cases, it may be sufficient to counter-irritate with iodine, the button cauter, or a fly-blister ; but generally *rest* should be insisted on, and the most effectual means of enforcing this is by putting on a long splint. Many cases in which rest has not been tried, and which have resisted every other local or general method of treatment, yield to the long splint. An inflammatory exudation is unquestionably apt to be increased by movement, and is most likely to disappear after rest with counter-irritation.

Poultices are of great service where the pain is severe, but blisters or the cauter produce a more powerful effect. Ice is recommended by some authors, but, if not actually harmful, is certainly unsatisfactory. A hypodermic injection of an eighth to a quarter of a grain of cocaine in the region of the nerve is most soothing, and is preferable to morphine ; the latter is indeed only permissible when the pain is agonising, and should never be administered by the patient himself. It must be always remembered that the risk that a sufferer from sciatica may acquire the morphine habit is considerable. Not infrequently an injection of distilled water or normal saline solution (Fleisch) into the nerve relieves the pain, and should be tried before resorting to morphine. Chloroform, absolute alcohol (Alexander), or 1 per cent osmic acid (2-10 minims) have been recommended for injection into the neighbourhood of the nerve, but they are hardly so serviceable, and this method of treatment is not free from the risk of increasing the interstitial exudation (Brissaud).

Acupuncture is a much-abused, but a very admirable, remedy. Not infrequently a patient, hardly able to walk on account of the pain, is almost instantaneously relieved by this method of treatment ; but a very chronic case is unsuitable. In practising acupuncture about six needles are required ; these should be at least two and a half inches in length.



The line of the nerve should first be marked out with ink or with a dermatographic pencil; then the needles, after being rendered thoroughly aseptic, should be dipped into carbolic oil (1 in 20), and rapidly inserted for about two inches (depending, of course, on the amount of fat and muscle to be penetrated), along the line of the nerve. Generally the highest needle is about the level of the fold of the buttock, and the lowest several inches above the popliteal space. Most of the needles actually pierce the nerve. If the operation be skilfully performed, the patient only perceives the first needle, and possibly the second; he cannot tell how many times he has been pricked, and has no conception that six long needles have been pushed into his thigh. The needles should be kept in position for an hour or thereabout, the limb being covered by a cage to keep off the pressure of the bed-clothes. Acupuncture is not employed nearly so frequently as it was years ago, but its usefulness in some cases should not be forgotten. Its *modus operandi* is probably the tapping of effusions in the nerve, and so relieving tension.

Baths are of great use in sciatica, and especially hot baths of all kinds. Hot under-current douches, in which, by means of a hose, hot water under considerable pressure is directed against the affected limb while the patient is seated or recumbent in an ordinary hot bath, are of service. Warm mud baths are also beneficial.

Electricity is not of great benefit. Galvanism has been recommended, one pole being applied to the sciatic notch, and the other to various points along the nerve; but the results are not very satisfactory. I have found the high-frequency currents of great value, but only a limited number of patients were cured completely by it alone (Worrall).

When all else fails, nerve stretching may be tried. The amount of tension brought to bear on the nerve should be sufficient at least to lift the limb off the table. One advantage is the breaking down of adhesions, which have much to do with the pain in cases of perineuritis. It is, however, unnecessary to stretch the nerve, and much better to investigate the position of the adhesions and to separate them. Many cases, incurable by other means of treatment, have yielded to this plan.

Massage for the muscles of the limb is desirable where there is any tendency to muscular atrophy. Tonics should be given in most cases; iron and arsenic being perhaps the best possible remedies for rheumatic subjects.

**Plantar Neuralgia.**—Occasionally, in place of sciatic neuralgia, the pain may be limited to a branch or branches of the nerve; very possibly in flat-foot the pain may be partly of neuralgic nature.

**Metatarsal Neuralgia, or Morton's Affection of the Foot.**—This peculiar affection, described first by T. G. Morton in 1876, is probably of neuralgic origin. It consists in spasmodic attacks of dull throbbing pain felt at the base of the fourth toe, sometimes of the second, and extending up the leg. It is increased by pressure over the head of the metatarsal bones, and, unlike rheumatism, is not specially severe at night.



*Etiology.*—Tight or badly fitting shoes exerting pressure on the heads of the metatarsals, especially on the fifth, may cause the condition in those otherwise disposed to neuralgia; and possibly much standing, in persons with a tendency to flat-foot, may be responsible in some cases. Morton's explanation was that the head of the fifth metatarsal being much shorter than the fourth was forced under the neck of the fourth, and might press on a terminal branch or branches of the plantar nerves. Oppenheim and others consider this simple explanation insufficient. The *treatment* is often very difficult. Broad shoes to prevent pressure over the heads of the metatarsals, or a bandage to support the plantar ligament where there is any tendency to flat-foot, may be efficacious in some cases; in others excision of the head of the metatarsal is the only certain and permanent cure.

**Paralysis of the Nerves of the Sacral Plexus.**—The sacral plexus, formed by the first three and part of the fourth sacral nerves, supplies the extensors and rotators of the hip, the flexors of the knee, and all the foot muscles; and it supplies the skin over the buttock, back of the thigh, outer side and back of the leg below the knee, and the greater part of the foot.

*Causes.*—The sacral plexus may be injured by diseases of the vertebral column or meninges, or by swellings compressing the nerve-roots, such as cellulitis, tumours in the pelvis, and, rarely, in parturition when forceps have been used in a narrow pelvis. Sometimes neuritis extends upwards from the sciatic nerve to involve the plexus, and possibly in a few rare cases it may arise primarily. When the cause of the paralysis is pelvic, the phenomena are generally more marked in the area of the external popliteal nerve. It is much more common to find particular nerves affected, or branches of these.

**Paralysis of the Small Sciatic Nerve.**—This nerve is rarely paralysed except from a lesion of the sacral plexus. It is entirely sensory and supplies the lower part of the buttock, the back of the thigh, and the upper part of the back of the leg, and it gives a branch to the perineum.

**Paralysis of the Sciatic Nerve.**—The same causes which paralyse the sacral plexus may paralyse the sciatic nerve alone. Among these causes pelvic tumours, instrumental delivery in narrow pelves, or even the pressure of the fetal head, are not uncommon; and, as mentioned above, the paralysis may be most marked in the area of the external popliteal branch. D. Gerhardt suggests that the fibres belonging to this nerve may be more susceptible to injury. Below the pelvis, wounds in the thigh, fractures or dislocations of the femur, tumours, hypodermic injections of ether and so forth, may be responsible. In not a few cases a neuritis of inflammatory origin or a toxic neuritis from alcohol, arsenic, lead, or other agents, may cause the paralysis.

*Clinical Features.*—The extensors of the hip, the flexors of the knee, and the muscles below the knee, may all be affected; or, if the lesion is situated below the middle of the thigh, the paralysis may be confined to the muscles last referred to. Not infrequently in a lesion of the whole

sciatic the external popliteal suffers more severely; and this is especially the case when the primary cause is situated in the pelvis.

The affected muscles may waste, and there may be a greater or less area of anaesthesia within the domain supplied by the nerve. Other trophic changes may occur, especially herpetic eruptions in the line of the nerve. If one sciatic is paralysed alone, the patient can still walk, because the quadriceps extensor cruris is able to fix the leg.

Where the branches of the sciatic are involved above the point of division of the trunk into the internal and external popliteal nerves, there will be loss of the power of external rotation of the thigh (the quadratus femoris, gemelli, and obturator internus), and paralysis of the flexors of the leg (the semi-membranosus, semi-tendinosus and biceps).

**Paralysis of the External Popliteal Nerve.**—This nerve supplies the long and short extensors of the toes, the peronei, and the tibialis anticus muscles. The sensory supply includes the outer side and front of the leg and the dorsum of the foot.

*Etiology.*—The nerve is very superficial where it passes over the head of the fibula, and hence may be injured by fractures of the head of the fibula, and by wounds and blows in that region. Powerful extension of the leg has set up neuritis; and in certain occupations in which there is much stooping, such as potato-picking or asphalt-laying, the nerve may suffer, possibly by pressure between the biceps tendon and the head of the fibula. Unquestionably alcoholism renders the nerve in such cases more susceptible to injury. There is sometimes a history of exposure to cold or a rheumatic family tendency.

*The clinical features* are marked foot-drop,—the ankle cannot be flexed, and the first phalanges of the toes cannot be extended; the gait is characteristically altered, the foot being raised in walking so that the toes may clear the ground. In old cases talipes equinus sets in; and generally, by contraction of unopposed muscles, the first phalanges of the toes become bent. There may be wasting of the affected muscles and anaesthesia of the area of skin supplied by the nerve. There may also be trophic changes as the result of paralysis of the nerve; bed-sores may form, and there may be abnormal growth of hair and nails.

**Paralysis of the Internal Popliteal Nerve.**—The nerve and its continuation the posterior tibial supply the muscles of the calf, the sole of the foot, the tibialis posticus, the popliteus, and the long flexors of the toes. The sensory supply includes the outer side of the lower part of the leg, the plantar aspect of the toes, and the sole.

*Etiology.*—The nerve may be injured by a wound or blow, sometimes by a strain; but it is much more commonly affected, along with other peripheral nerves, by toxic agents.

*Clinical Features.*—Extension at the ankle-joint, flexion of the toes, and the ability to stamp on the ground are all lost. The patient cannot rise on tip-toe, and, as time goes on, talipes calcaneus sets in, and the toes, from secondary contraction, become claw-like. There may be

wasting of the affected muscles, and more or less definite anaesthesia in the area supplied by the affected nerve.

**Paralysis of the Plantar Nerves.**—These nerves rarely suffer alone, unless from direct injury. The internal plantar supplies the flexor brevis digitorum, the plantar muscles of the great toe (except the abductors), and the first lumbrical muscle; whilst the sensory supply includes the inner side of the sole and the inner three and a half toes.

The external plantar supplies the flexor accessorius, the adductor of the great toe, all the plantar muscles of the little toe, all the interossei, and the outer three lumbricals; whilst the sensory supply includes the outer half of the sole and the outer one and a half toes.

Paralysis of the external plantar very seriously interferes with walking, as pointed out by Sir W. Gowers; the toes cannot aid propulsion of the body forwards, and the interossei being paralysed the toes become flexed at the two distal, and extended at the proximal, phalangeal joints.

**Neuralgia of the Genitals and Rectum.**—Sometimes there is neuralgia in the testicle or spermatic cord, with hyperaesthesia of skin, and, not infrequently, spasm of the cremaster muscle: more rarely priapism, and even discharge of semen are observed during the attacks of pain, and the affected testicle may swell. Generally a suspensory bandage and ordinary anti-neuralgic remedies are sufficient to effect a cure. In women the clitoris or labia may be the seat of neuralgic pain. Neuralgia may be of perineal or more commonly of rectal origin. Perineal neuralgia is sometimes associated, as testicular and prostatic neuralgia may be, with masturbation. Rectal neuralgia may be caused by a loaded rectum, by fistula or fissure, or any rectal irritation; but often rectal, perineal, testicular, and urethral neuralgic pains are more or less mental in origin; and not a few of these sufferers find their way eventually to an asylum. It must not be forgotten that the vesical and rectal crises of tabes are really neuralgic. In tabetic women there may also be vulvo-vaginal or, according to some authorities, crises associated with the clitoris. Ovarian neuralgia is common in gynaecological practice, and a description of its causes, nature, and treatment should be sought in special works on diseases of women.

**Coccygodynia; Coccygeal Neuralgia.**—This generally occurs in women, and consists in a severe pain in the region of the coccyx, which is caused by any pressure on it, or by contraction of muscles connected with it, such as may be produced by sitting, going to stool, or even by the muscular effort of passing urine. It may follow a severe labour, or an injury to the spine; and is especially common in the subjects of hysteria. It may be a simple neuralgia; or there may be an inflammatory condition of the coccyx and the muscles and other structures attached to it, especially when the pain follows an injury (Rohleder).

Anti-neuralgic treatment, opium or cocaine suppositories, and sometimes electricity, may be sufficient to effect a cure; or it may be necessary to resort to operative interference, either removing the coccyx or separating the bone from its attachments to surrounding tissues.



**Paralysis of the pudendal and coccygeal plexuses** may result from injury to the lower part of the spinal column, as by a fall from a height. It may be due to inflammatory lesions of the lower part of the spinal cord or the region of the conus medullaris; and syphilis bulks largely as a causal factor. Tumours may also be present in the sacral canal and compress nerves. As a rule, the bladder and rectum are paralysed, and pain which radiates from the sacral region may be felt in the neighbourhood of these organs. The skin of the perineum and genital organs, however, is anaesthetic.

The *prognosis* depends on the improvement brought about by the administration of antisymphilitic remedies and the possibility of an operation in cases which are not specific, so as to remove a tumour or other cause of pressure. Persistent paralysis of the bladder adds the dangers of a catheter life and increases the gravity of the case.

G. A. GIBSON, }  
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## DISEASES OF THE CAUDA EQUINA

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**Anatomy.**—The spinal cord is considerably shorter than the spinal canal and the dural sheath, and terminates at the lower border of the body of the first lumbar vertebra. At this level, the *conus medullaris* really represents the lowest part of the spinal cord proper, and rapidly diminishes in size. The apex of the cone gives off a slender filament, the *filum terminale* or central ligament of the cord, which is surrounded by a mass of nerve-roots, beginning with the second lumbar, on their way to their respective canals of exit. This collection, inside the theca, of lumbar and sacral nerve-roots surrounding the *filum terminale* constitutes the cauda equina. The *filum terminale* is 17 to 18 cm. in length, and reaches the lower end of the sheath opposite the second sacral vertebra, where it perforates the dura mater, and, receiving a covering from it, becomes attached either to the periosteum of the lower end of the sacral canal or to the back of the coccyx. The portion within the common



sheath of dura mater is sometimes distinguished by the name *filum terminale internum*, whilst below this sheath, and where it is blended with the dura mater, it is called the *filum terminale externum* or the *filum duræ matris spinalis*. The filum consists of pia mater enclosing for about half its length what in reality is the continuation of the central canal of the cord, with a little surrounding grey matter near its upper end. Below the end of the central canal the filum is mainly composed of connective tissue enclosing branches from the anterior spinal arteries, and three or four small bundles of medullated nerve-fibres with a few ganglion-cells, which Rauber regarded as the undivided coccygeal nerve-roots. Its silvery appearance at once distinguishes the filum terminale from the surrounding nerve-roots. As the central canal of the spinal cord is the

remains of the embryonic structure from which the spinal cord develops, it is naturally more obvious in the fetus and less distinct as development goes on, and in the adult may be obliterated in several places.

**Etiology.**—From an analysis of 100 cases of disease of the cauda equina, Dufour finds that *injury* is by far the most frequent etiological factor. When the first lumbar vertebra is damaged the conus medullaris suffers; a lesion of the second lumbar vertebra may implicate either the conus medullaris or the cauda equina; and in damage to vertebrae below the second lumbar, the cauda equina alone is affected. The nature of the lesion is fracture or dislocation of vertebrae, sometimes due to violence and sometimes to a fall from a height. Injury may also be due to bullet wounds. Tumours of bones or of the meninges are the next most important cause of disease of the cauda equina. The tumours may be sarcoma, carcinoma, or rarely fibro-sarcoma, nenroma, or glioma. Dufour mentions 8 cases of hydatid cysts in the region of the cauda equina. Haemorrhage, gumma, meningitis, and abscess due to tuberculous disease of bone are probably responsible for most of the remaining cases. In rare instances the nerve-roots of the cauda equina may be expanded over the sac of a spina bifida.

**Symptoms and Signs.**—As the cauda equina includes not only the lumbar nerve-roots beginning with the second and all the nerves of the sacral and coccygeal plexuses, but also the anterior and posterior roots, the resulting changes will vary according to the level of the lesion, and

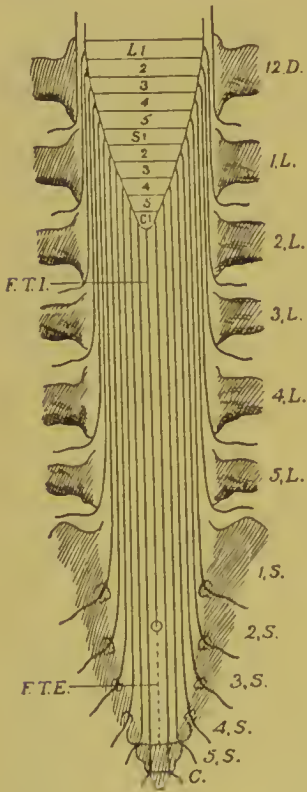


FIG. 68.—Sketch of the conus medullaris indicating the spinal segments into which it is divided. It shows the lumbar, sacral, and coccygeal nerve-roots surrounding the filum terminale. F.T.I., filum terminale internum; F.T.E., filum terminale externum.



whether the anterior or the posterior roots or both are implicated. The distribution of sensory and motor symptoms follows the distribution of a root instead of a nerve lesion. The clinical features of a lesion of the cauda equina may be readily appreciated from a study of the accompanying table, which, as suggested by Dr. Warrington, shews the observations made by Raymond and Seiffer placed side by side.

TABLE

	Motor.	Reflexes.	Sensory supply according to Raymond.	Sensory supply according to Seiffer.
5th Lumbar.	Glut. med. and min., Tens. fasc. femoris, Semi-membran., Semi-tendinosus, and Biceps.	...	Outer side of thigh.	Ext. surface of leg, dorsum of foot, sole of foot.
1st Sacral.	Pyriformis, Obt. internus, Gemelli, Glut. max.	Plantar.	Posterior surface of thigh and leg.	Ext. surface of leg, dorsum and sole of foot, outer part of posterior surface of leg.
2nd Sacral.	Tib. ant., Peroneal muscles. Centre for micturition.	...	External surface of leg and of foot. Sensation of bladder and upper part of rectum.	Median part of posterior surface of thigh.
3rd Sacral.	Centre for ejaculation, Ischio- and Bulbo-cavernosi.	...	Sensation of urethra, penis, and scrotum.	Penis, scrotum, vulva, perineum, and region of buttocks.
4th Sacral.	Muscles of bladder.	Ankle-jerk.	Perineum and sacral region.	An oval area, including the region of sacrum as far as anus.
5th Sacral.	Levator ani. Sphincter ani.	Anal.	Coccygeal region. Anus.	...

A complete lesion of the cauda equina gives rise to flaccid paralysis with atrophy of the leg muscles supplied by the branches of the sacral plexus and by the lumbar roots below the second, and to high-steppage gait due to marked foot-drop. The affected nerves shew diminished excitability both to faradism and galvanism, and the reaction of degeneration may be obtained in the muscles. There is pain, generally very

severe and of gradual onset, in the region of both sciatics; so that the patient may complain of double sciatica. There is anaesthesia over a saddle-shaped area in the gluteal region, and usually a strip of anaesthesia can be made out on each side at the back of the thigh, and, as described in the table, there is anaesthesia of the outer side of the leg and foot. There is anaesthesia of the mucous membrane of bladder, urethra, and rectum, of the penis and serotum in the male, and of the vulva and vagina in the female, and also of the perineum. There is paralysis of bladder and rectum with diminution and probably complete loss of sexual power. Bed-sores may appear. The Achilles, plantar, anal, and bulbo-cavernosi reflexes are abolished, whilst the knee-jerks are retained.

According as the first, second, or third lumbar roots escape, the area of anaesthesia diminishes from above downwards. When the lesion involves merely the two lower sacral and the coccygeal roots there is paralysis of the levator ani, with anaesthesia of the skin of the anus and perineum.

**Diagnosis.**—Many symptoms may occur both in affections of the conus and in diseases of the cauda equina, but it is of the utmost importance that a differential diagnosis should be made, for whereas lesions of the conus are usually inoperable, in not a few cases of disease of the cauda equina alone the surgeon can effect partial, if not complete, cure.

In the conus medullaris, which is of very small extent, many nerves originate, and hence a lesion affecting it must rapidly produce the maximum amount of damage. In lesions of the cauda equina, on the other hand, the symptoms come on more gradually. There is usually more violent pain, which is apt to be excited by any change of position. Pain over the vertebral column below the level of the second lumbar spine, and pain which radiates towards the legs and is increased by percussion or pressure over the vertebrae, favours a lesion of the cauda equina. Pain at a higher level, although increased by pressure but not radiating towards the legs, favours a lesion of the cord. In affections of the cauda equina the pain is usually referred into the course of the sciatic nerves, and it is more severe and lasts longer than in diseases of the conus medullaris. The presence of what is known as Lasègue's sign points to a lesion of the cauda equina, or at least of the associated nerve-roots. This sign consists in the production of pain when an attempt is made to flex the thigh on the pelvis with the leg extended. Want of symmetry in the symptoms and signs is in favour of a lesion of the cauda or of the nerve-roots, and any improvement as regards paralysis of the bladder or bowels is more likely to be associated with disease of the cauda. The slow development of muscular atrophy, the reaction of degeneration, and other trophic disturbances also indicate a caudal lesion. According to Oppenheim, well-marked anaesthesia favours a lesion of the conus medullaris, and Schultze believes that anaesthesia to pain and temperature, but not to tactile sensation, also indicates a lesion of the conus.

The **prognosis**, as already stated, is much better in lesions of the cauda than of the conus medullaris. Mr. Thorburn and others have operated with success in cases of fracture, and in a steadily increasing

number of cases tumours of all kinds have been removed with good results. In specific cases antisyphilitic treatment should be adopted, but the best results have been obtained in cases suitable for operation.

**Treatment** can be very briefly dismissed, for, apart from antisyphilitic remedies, it is purely surgical. It is not, however, improbable that in some tuberculous cases the use of tuberculin may be beneficial. Valuable records of cases mostly treated by operation have been reported by Cassirer, Ferrier and Horsley, and Thorburn and Warrington (*vide* also p. 877).

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### MULTIPLE SYMMETRICAL PERIPHERAL NEURITIS

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**Introduction.**—The name neuritis is usually understood to mean inflammation of a nerve; but, as pointed out by Dr. T. Buzzard, this is not its original interpretation. The adjective neuritis, the substantive *νόσος* being understood, signifies etymologically no more than disease affecting the nerve. It has indeed become customary, and even necessary, to include under the name neuritis not only what is ordinarily called inflammation, but also degeneration, atrophy, and other lesions of a nerve. Some of the chief characteristics of the affection to be considered in the present article are indicated by qualifying epithets. Thus, *peripheral* indicates that the extremities of the nerves are most markedly affected; *multiple* that many nerves are affected; and *symmetrical* that corresponding nerves on the two sides of the body are attacked, often almost simultaneously.

The commonest cause of the disease is a chemical poison: and it is important at the very outset to recognise (i.) that the action of the poison is not necessarily limited to the peripheral nerves; on the contrary, there are frequently indications that it has impaired the functions of other

parts of the nervous system ; (ii.) that the name Peripheral Neuritis does not imply that the abnormal condition of the nerves, upon which the characteristic symptoms appear to depend, is due to the direct action of the poison, and is entirely independent of changes produced by the poison in the central nervous system. In other words, lesions of the peripheral nerves do not necessarily constitute the whole anatomical substratum of the disease, but are its most conspicuous features.

**History.**—The clinical features of multiple neuritis are described by many of the older observers. Thus, admirable descriptions of alcoholic paralysis were given by Lettsom in 1789, and by J. Jackson in 1822 ; but Graves was probably the first to suspect that certain forms of generalised paralysis depend on disease not of the brain or spinal cord, but of the nervous cords themselves. “One of the most remarkable examples of disease of the nervous system commencing in the extremities and having no connexion with lesions of brain or spinal marrow,” he says, “was the curious *épidémie de Paris* which occurred in the spring of 1828.” After describing the chief symptoms and progress of this epidemic, the author says, “Now here is another remarkable instance of paralysis creeping from the extremities towards the centre. Here is a paralysis affecting all parts of the extremities as completely as if it had its origin in the central parts of the nervous system ; and can any one, with such palpable evidence before him, hesitate to believe that paralysis or even hemiplegia, without any lesion of the brain or spinal cord, may arise from disease commencing and originating in the nervous extremities alone ?” In another passage Graves asks the question : “May not the decay and withering of the nervous tree commence occasionally in its extreme branches ? And may not a blighting influence affect the latter, while the main trunk remains sound and unharmed ?” Todd, too, appears to have recognised that lead palsy depends on disease of the nerves. In one of his clinical lectures he says : “I believe that the muscles and nerves are early affected, and that at a later period the nerve centres become implicated. The nervous system is thus first affected at its periphery, in the nerves, and, the poisonous influence continuing, the contamination gradually advances towards the centre.”

The first case, however, in which the presence of neuritis was proved after death was published by Duménil, of Ronen, in 1864. The patient was a tailor, aged sixty-one years, who presented the symptoms now recognised as characteristic of peripheral neuritis ; and the necropsy revealed disease of the small nerves of the hands and feet, the brain and cord being quite healthy. In 1866 Duménil made a second communication on peripheral paralysis, and reported another case with necropsy. These important pathological observations appear to have attracted little notice ; and it was not until further observations were reported by Lancereaux in 1871, Eichhorst in 1875, Joffroy in 1879, Leyden in 1880, and Grainger Stewart in 1881, that the doctrine of peripheral neuritis was placed upon a sure pathological basis. The degeneration of the nerves of the palate in a case of diphtheritic paralysis, discovered by



Charcot and Vulpian in 1862, and the changes described in the muscles and nerves taken from a case of lead paralysis by Lancereaux in 1871 threw much light on this subject.

During the last twenty-five years many observations and monographs relating to the subject of peripheral neuritis have been published; it would be impossible, within the limits of the present article, to enumerate even the more important of them; but I would draw attention to the work of Moeli, Leyden, Remak and Flatau in Germany, of Ballet, Dejerine, Raymond, Pitres and Vaillard in France, and of Dreschfeld, T. Buzzard, and Ross in this country. The late Prof. Dreschfeld was the first in England to adduce anatomical evidence in favour of the neuritic hypothesis of alcoholic paralysis. The very interesting and valuable series of cases which formed the basis of the Harveian lectures delivered by Dr. T. Buzzard in 1885, gave a great impetus to a careful study of the subject; whilst Ross's suggestive classification of peripheral neuritis, in which for the first time prominent places are given to an irritative and a vasomotor type, greatly enlarged our field of inquiry, and gave a more definite view of the clinical features of the disease. Scientific discoveries are perhaps seldom followed by any immediate benefit to humanity. It is therefore gratifying to notice that the discovery by my colleague, Dr. Reynolds, that arsenic was the chief cause of the epidemic of peripheral neuritis in 1900, led to the avoidance of much suffering and to the saving of many lives.

**Classification.**—A study of peripheral neuritis brings out very clearly that in most cases the cause of the disease is some kind of poison. Hence it has been found convenient to classify its different forms according to our knowledge of the causes producing them. Thus, peripheral neuritis may be caused by lead, arsenic, mercury, phosphorus, or silver; by alcohol, ether, bisulphide of carbon, dinitro-benzol, aniline, or carbon monoxide. It may also be caused by the micro-organisms which produce specific diseases, or by their products: for example, those of diphtheria, influenza, enteric, and other fevers; of pneumonia, erysipelas, gonorrhoea, syphilis; of the various forms of septicaemia (including puerperal infections) and malaria. Of beriberi and leprosy it is an essential part, and it occurs, too, in rheumatism, gout, and diabetes. It is not improbable that the cases of peripheral neuritis, associated with anaemia, pregnancy, the cancerous and other forms of cachexia, and gastro-intestinal disturbance, and after over-fatigue and exposure to cold and wet, also owe their origin to some toxic agent.

An etiological classification is useful in bringing into prominence the fact that variations in the symptoms of peripheral neuritis are partly due to variations in the selective action of different poisons. Thus, lead picks out certain branches of the musculo-spiral nerves, whilst alcohol shews a preference for the nerves supplying the flexors of the ankle.

It is, however, to be noted that no particular set of symptoms is exclusively related to a particular poison. Moreover, in practice the first question to be answered is not what poison has injured the nervous

system, but what part of the nervous system is affected ; have we to deal mainly with disease of the peripheral nerves, or with disease of the central nervous system ? In other words, we have first to diagnose the presence of peripheral neuritis, and then to seek its cause ; indeed, it is not until we have mastered the symptomatology of the disorder that we can make a satisfactory inquiry into its causation.

I have therefore determined to adopt a classification which seems to be both more logical, and also, from a clinical point of view, more desirable. I am also induced to treat the subject from a broad standpoint and to give an account of certain forms only of multiple neuritis, partly because the limits of space do not permit an adequate description of every variety, and partly because the relations of neuritis to many of its causes have already been considered in various parts of this *System of Medicine* (see diphtheria, leprosy, beriberi, metallic and other poisons, etc.). Taking the commonest example of multiple neuritis, namely the alcoholic variety, as our guide to classification, we shall find the characteristic clinical feature to be symmetrical localisation of motor, sensory, and vasomotor symptoms in the peripheral parts of the limbs. As a rule all these symptoms are present, though varying much in relative intensity in different cases, and at different stages of the disease. Careful clinical observations also shew that any one of the three groups of symptoms may predominate, and in exceptional cases be present alone. It is not, indeed, uncommon to see cases of alcoholic paralysis in which sensation is quite normal to the most careful testing ; and occasionally cases occur in which sensory or vasomotor symptoms, if not present alone, are at any rate the most conspicuous features.

Furthermore, if we consider the symptoms of alcoholic neuritis at different stages of the disorder, we find that symptoms indicative of irritation of nerve-tissue are present in the early stages of the disease, and that symptoms indicative of destruction of nerve-tissue are present in the later. Thus, in the early stages we have, on the motor side, muscular spasms and cramps ; on the sensory side, shooting pains, paraesthesia, and cutaneous and muscular hyperaesthesia ; in the later stages, paralysis and anaesthesia are predominant. Now in some cases irritative phenomena are present alone from first to last, the motor being prominent in one set of cases, the sensory in another set. If, then, we meet with cases, alcoholic or other, in which muscular spasms or irritative sensory or vasomotor phenomena are the dominant features, and are symmetrically localised in the extremities, can we adduce evidence that such cases are really examples of peripheral neuritis, using the name, in the wide sense already proposed, to denote any abnormal condition of the peripheral nerves ? In the course of this article this question will be discussed. In the meantime, the above considerations suggest the following simple classification as a basis for practice :—

- I. *The common or mixed type* ; motor, sensory, and vasomotor phenomena being present in various combinations. Examples : alcoholic paralysis, arsenical palsy.

- II. *The motor type* ; motor phenomena are dominant or alone.
- (A) The spasmodic variety, reaching its maximum in tetany.
  - (B) The paralytic variety ; under which head are included chronic local forms of paralysis, as exemplified by lead neuritis ; and acute universal forms of paralysis, as exemplified by some varieties of Landry's disease.
  - (C) The atrophic variety, in which the degree of paralysis appears to depend on the amount of muscular atrophy present.
- III. *The sensory type*.
- (A) Sensory symptoms exist alone, or in association with a varying amount of muscular weakness.
  - (B) Sensory symptoms are associated with muscular inco-ordination ; this variety is sometimes called neuro-tabes peripherica.
- IV. *The vasomotor type*.—Raynaud's disease (*vide* p. 120), Erythromelalgia (*vide* p. 149).

### I. THE COMMON OR MIXED TYPE

ALCOHOLIC POLYNEURITIS.—Before the epidemic of neuritis from arsenical beer in 1900 it was assumed that neuritis in an alcoholic subject was due to the action of alcohol on the peripheral nerves. Doubts as to the correctness of this assumption were raised by the discovery of arsenic in the beer and by the views expressed by Dr. Reynolds. The epidemic drew attention to the importance of considering not only whether neuritis in a drinker might be due to the presence in his beverage of some poison other than alcohol, but also whether alcohol by itself could cause neuritis. In his account of the epidemic Dr. Reynolds stated: "I have for many years doubted whether ethylic alcohol *per se* does cause peripheral neuritis at all, and I have personally felt more and more confirmed in this opinion each succeeding year." Again, in replying to the discussion on his paper read at the Medico-Chirurgical Society, he said, "I am willing to admit that alcoholic neuritis exists, but I am not convinced thereof," and he threw out the suggestion that all cases of so-called alcoholic neuritis might be really due not to alcohol but to arsenic. More recently he has stated that he never meant to deny the existence of alcoholic neuritis, but his belief is that it is rare and usually slight in degree. These statements are so contrary to the generally accepted views that they must be briefly considered. If arsenic were the chief cause of so-called alcoholic neuritis there naturally would be a great diminution in the number of cases occurring after the epidemic, that is, when the beer was free from arsenic. On the contrary, the percentage of cases admitted to the Manchester Royal Infirmary since the epidemic is almost equal to that of the cases admitted before the epidemic, being about 1 per cent in the former and 1·1 per cent in the latter. But in 1900, the year of the epidemic, there were 62 cases out of 1343 medical in-patients, or 4·6 per cent. Hence it



is clear that, before and after the epidemic, arsenic, if present at all in the alcohol consumed, was in very small quantities. Further, it is to be noted that pigmentation, keratosis, and other cutaneous lesions, so prevalent in the epidemic, were not mentioned in the reports of earlier cases by such acute observers as Ross and Dreschfeld. On the other hand, we must admit that the majority of the Manchester cases have been in beer-drinkers, and that a small amount of arsenic in the beer may have been a contributory factor.

It is therefore desirable to consider the question of neuritis in drinkers of spirits. In this connexion we may note the valuable statistics of Dr. F. Buzzard. In the ten years 1891-1900, out of 6458 cases admitted to the National Hospital there were 108 cases of alcoholic neuritis, that is 1.6 per cent. Of these 108 cases, 25 were due to excess in spirits only, and one case only was due solely to beer. Dr. Buchan also, in 19 cases of alcoholic neuritis, found that whisky was the chief beverage in 18, and the only one in 6. These results are in accordance with the records of the earliest observers of peripheral neuritis in alcoholic subjects, witness the graphic account by Lettsom of the disease as occurring in those who drank brandy and gin in excess, and that by James Jackson, who attributed the disease to ardent spirits. They are also borne out by the statements of modern authorities on the subject. Thus, Dr. T. Buzzard says his experience has been that neuritis is due especially to spirit-drinking. Ross, in an analysis of 90 cases, found that the form of alcoholic beverage was as follows:—in 22 spirits, in 3 absinthe and vermouth, in 13 beer and spirits, in 5 beer only, whilst in 47 the kind of alcohol was not given. Moreover, of recent years many cases of peripheral neuritis from spirit-drinking have been observed in which beer could be definitely excluded. Dr. R. T. Williamson has recorded a case from excessive whisky-drinking—no beer having been taken—in which the diagnosis was verified by a microscopical examination of the peripheral nerves. In this case three samples of the same whisky gave no reaction for arsenic with Reinseh's test. Reverting to the question of beer-drinking I may mention that several cases of well-marked multiple neuritis which have come under my care since the epidemic have been carefully investigated, and arsenic as an etiological factor definitely excluded, no trace of this poison being found in the hair or the urine of the patients nor in samples of the beer that had been taken. Quite recently Prof. Dixon Mann assured me that he was quite satisfied as to the existence of true alcoholic neuritis.

It is open to any one to say that it is not the ethylic alcohol, but some accidental impurity that is responsible for the neuritis, but until this toxic agent is discovered, and it certainly is not arsenic, it is impossible to resist the conviction that alcohol, whether in the form of beer, wine, or spirits, is a common cause of multiple neuritis. But this statement does not necessarily imply that multiple neuritis is frequent in alcoholic subjects, nor that the disease is a direct result of alcohol. Indeed, the proportion of alcoholics who suffer from neuritis is small, and



in such sufferers other factors may play a contributory part. The action of alcohol may be an indirect one in the production, not only of neuritis, but of hepatic cirrhosis and of changes in the muscle of the heart. It is a reasonable assumption that the lowering of tissue-resistance by alcohol permits the successful attack of toxins, derived from micro-organisms or from the changes associated with chronic inflammation, upon the nerves, liver, heart, or other structure. A similar view is held by Dr. F. Parkes Weber, who suggests that the true causes of multiple neuritis of the alcoholic type are infections, alcohol being merely a disposing agent. But whether the neuritis is a direct or an indirect result of the poison, ample evidence has been adduced to justify the retention of the term alcoholic polyneuritis.

*Age.*—By far the majority of the patients are between thirty and fifty years of age; the affection is seldom met with under twenty or over sixty years. Occasionally, however, it occurs at the extremes of life. Thus, Herter records a remarkable case of acute alcoholic intoxication in a boy aged three years. The child, after a large drink of whisky, suffered from convulsions and paralysis of cerebral origin; and subsequently from typical symptoms of multiple neuritis. He made a complete recovery. As an instance of alcoholic neuritis at advanced age, Dr. Maude's case of a man aged seventy-six may be mentioned.

The severer degrees of alcoholic neuritis are common in women, but the milder are met with as frequently in men.

*Morbid Anatomy.*—The results of necropsies in cases of alcoholic paralysis shew that, whilst morbid changes are frequently found in the brain and spinal cord, the most constant changes are in the peripheral nerves; and there is now abundant evidence in favour of a direct causal relation between peripheral nerve changes and the peripheral paralytic phenomena.

The changes in the *nerves* may involve both the connective tissue and the nerve-fibres, but the latter always suffer more severely. The condition then is mainly one of parenchymatous neuritis; perineuritis and interstitial neuritis being absent, or present to a slight degree only. Hence, to the naked eye the nerves and their branches appear quite healthy. In acute cases, however, when there has been acute inflammation of the sheath and connective tissue, the nerve may appear reddened and swollen; or, at a later stage, soft and pulpy. The microscopical changes have already been described on p. 362. As regards the distribution of the changes in the nerve-fibres the rule is that they are most intense in the terminal branches to the muscles and skin, and become progressively less marked towards the larger branches; the trunk and anterior roots of the nerve are usually quite healthy.

In the diseased portions of the nerve the fibres are not affected equally; some may be quite normal, some may be slightly affected, others may have undergone complete atrophy. These differences, as shewn by Dr. Fleming, are largely related to the presence or absence of local exudations in consequence of changes in the vessels.

The nerves of the limbs are principally affected, and, whilst all the terminal nerves of the limbs may be involved in some degree, the branches of the musculo-spiral and the anterior tibial usually suffer most. Degenerated fibres have also often been found in the phrenic and vagus nerves.

The *muscles* in connexion with diseased nerves present changes similar to those in experimental neuritis: they are pale and wasted, and their fibres are reduced in size. All the fibres are not affected to the same extent, and the variations are greater than in cases of experimental neuritis. There are changes, too, which appear to depend on some process other than simple atrophy. Thus, the connective tissue of the muscles may be profoundly altered; its overgrowth in some cases is so great that it looks as if there had been a primary fibrosis of muscle with a secondary atrophy of its fibres. This interstitial myositis is chiefly found in cases of chronic neuritis, but it may appear in acute cases. Two causes may be suggested: that it is secondary to the irritating effects of the poison on the nerve branches; or that it is primary, and due to the action of the poison on the muscle itself.

The *spinal cord* has been found healthy in many cases, even when carefully examined by the most recent methods of investigation.

In other cases of alcoholic neuritis, changes have been found in the cord. As Dr. Tooth has pointed out, the cells of the anterior horns, although generally unaltered in form, may shew heavy pigmentation. He says that the pigment in the cells of normal cords increases in quantity and depth of colour as the age increases; and he regards the heavy pigmentation referred to as a hint that premature old age of the cord may follow chronic alcoholism. But, in addition to increased pigmentation, the cells may present a vitreous appearance, or distinct vacuolation. In many cases disappearance of Nissl's granules has been observed together with a lateral displacement of the nucleus. These changes may be secondary to those in the peripheral nerves (*réaction à distance* of Marinesco), or both cells and nerve-fibres may be affected simultaneously. More considerable changes have also been found: namely, chronic inflammation of the membranes, especially of the pia mater; an irregularly disseminated chronic myelitis; and in some cases an overgrowth of connective tissue throughout the cord, often especially marked in the posterior columns. Slight degeneration of the columns of Goll is frequently mentioned in reports of cases of alcoholic neuritis.

Similar degenerative changes in the large cortical cells of the brain are also common, and to these cortical changes the mental disorder is doubtless closely related (*vide* pp. 228, 230).

Many other poisons, enumerated above as causes of peripheral neuritis, may produce what we have called the common or mixed type. Two, namely arsenic and the poison of beriberi, may be specially mentioned as giving rise to symptoms which closely resemble those of alcoholic paralysis.

**Symptoms.**—The complaints of a patient in the early stage of chronic

alcoholic poisoning may usually be referred to disorders ( $\alpha$ ) of the digestive, ( $\beta$ ) circulatory, or ( $\gamma$ ) nervous systems.

The subjects of the first group complain of morning retching and vomiting, and of abdominal pain or disturbed action of the bowels; an examination reveals evidence of congestion and catarrh of the mouth and pharynx. The subjects of the second group complain of shortness of breath on exertion, and sometimes of dropsy; on examination the heart is found dilated. The subjects of the third group complain of numb or cold extremities, and of cramps or muscular weakness; or of symptoms, such as impaired memory, which indicate disturbance of the cerebral functions. Each of these groups of symptoms is met with in practice, either separately or in combination with the other groups, as the results of chronic alcoholism. Thus, a patient may suffer for a long period from dyspnoea, dropsy, and congestion of the liver, and yet be entirely free from any nervous symptoms; on the other hand, paralysis and mental impairment may steadily set in without any decided symptoms of gastric or cardiac disturbance. These differences depend on the varying susceptibilities of the tissues of different individuals to alcohol, rather than on the kind of alcoholic drink indulged in. On the other hand, signs of slight degrees of neuritis may frequently be found in what may be called the *gastric* and *cardiac* types of alcoholism, as well as in cases of ascites from cirrhosis of the liver.

*Mode of Onset.*—In a few cases the onset of paralysis is quite sudden, as in the case of a man who, when smoking, found himself unable to lift up his hand to take his pipe from his mouth; but, as a rule, paralysis not only sets in insidiously, but is preceded by certain premonitory symptoms which have existed in varying degrees of intensity for many weeks, months, or even years. These are not separated abruptly from the symptoms of the fully established disease; indeed, they are often present during its whole course. Nevertheless it is desirable to give them a prominent place at the outset, because they are very frequent, and often appear long before any signs of paralysis, and at a time when the knee-jerks, instead of being absent, are either normal or exaggerated.

The symptoms I refer to are disorders of the tactile sensibility of the extremities, vasomotor irregularities, and muscular spasms. The *disorders of tactile sensibility* are usually described by the patient as numbness and tingling, or “pins and needles,” in the fingers and toes. The hands feel as if covered with gloves, and the feet as if something soft, like fur or wool, intervened between the soles and the ground. Patients in this state have frequently to rub their hands together several times before they are able to use them for writing, sewing, or other work. The *vasomotor disorders* consist of cold hands and feet, and sometimes of hot, burning sensations in the extremities. A patient may notice that on getting up in the morning his fingers go of a dark livid colour; or that, when his feet are hanging down, the soles and the toes turn dark red. *Muscular spasms* may be present, in the form of tremors and twitchings of the extremities; but more frequently they appear as active cramps, which are



most severe and persistent in the calves of the legs. These cramps are usually very troublesome at night, just as the patient is about to fall asleep, or in the early morning; he feels that the calf is drawn up into a lump, and is often obliged to get out of bed and press his toes on the floor, rubbing first one calf and then the other for some time before the spasm relaxes. Sometimes the flesh is so sore that he prefers to bear the cramp rather than suffer the pain of the rubbing.

*Sensory Disorders.*—In addition to “numbness and tingling,” patients also suffer from pains of various kinds, which occur most commonly and severely in the early stages of the disease, but are by no means confined to that period. They may be aching, burning, twisting, or shooting in character. Paroxysms of excruciating lancinating pains in the limbs, especially in the lower limbs, frequently deprive the patient of rest and appetite, and thus become important contributory factors in the general weakness and emaciation which characterise severe cases of alcoholic paralysis. At one time the patient has darting pains in the instep or in the sole of the foot, at another in the fingers, at another along the course of the sciatic nerves; in other cases, again, the sensory branches of the cervical or brachial plexuses, or the nerves of the trunk, are implicated. The plantar nerves are very liable to be affected, and then the soles of the feet become sensitive to pressure, and cause the patient much distress in walking. In such cases certain parts of the sole are particularly tender, as at the centre of the heel, where the internal plantar nerve leaves the fascia to become superficial; and over points between the ends of the metatarsal bones where the nerve divides into its digital branches.

Some of the visceral nerves are occasionally the seat of neuralgic attacks. Thus, the patient may be subject to griping intestinal pains, like lead colic; or to paroxysmal attacks of severe gastralgia which, when associated with vomiting, may closely resemble the gastric crises of tabes. Of the objective sensory phenomena, the sensibility of the skin, muscles, and nerves requires careful investigation. Besides the tenderness of the soles of the feet, spots of cutaneous hyperaesthesia may be found also on the forearms and legs. The superficial nerve-trunks, such as the musculo-spiral, the ulnar or the popliteal, may be unduly sensitive, and sometimes even enlarged. But the most frequent and prominent sensory phenomenon in alcoholic neuritis is muscular hyperaesthesia. This is usually most marked in the calves of the legs, but is present in other muscles of the limbs also; in slight degrees of tenderness the patient shrinks when the muscles are gently squeezed, and in severe cases he is unable to bear the slightest movement or pressure, so that even the weight of the bed-clothes may be intolerable, and the feet and legs have to be protected by cradles. Cutaneous anaesthesia, although a less prominent symptom than muscular hyperaesthesia, is usually present in some degree. It is more common to meet with loss of sensibility to painful impressions than to tactile; sometimes the sense of temperature is impaired also, all objects feeling cold; or cold and hot bodies are not readily distinguished. As a rule, anaesthesia is partial, but it may be



complete ; it is found in the lower limbs as high as the knees, in the upper limbs as high as the elbows ; and occasionally in the arms and thighs. Cutaneous anaesthesia and muscular hyperaesthesia often coexist in advanced stages of the disease ; in the early stages either may exist alone. In fact, any disorder of sensation may be present at any period of the disease, and the chief points to bear in mind are—(i.) That numbness and tingling and aching and shooting pains are early symptoms ; (ii.) that muscular hyperaesthesia and cutaneous anaesthesia characterise the fully established disease ; (iii.) that anaesthesia is very variable both in intensity and extent ; in some cases the most careful examination being required to detect it, whereas in others it is completely absent.

*Motor Disorders.*—The tremor, twitching, and cramps which constitute the premonitory and early symptoms of alcoholic neuritis are also present, in varying degree, during its whole course. In addition to these symptoms of morbid overaction of muscular tissue, the further progress of the disease is indicated by muscular weakness, which, beginning usually in the periphery, gradually spreads to the proximal segments of the limbs and, in some cases, to the muscles of the trunk. At first the patient finds that he is losing his spring in walking, or that he has a difficulty in ascending a stair ; and he may also have noticed that he cannot execute certain special actions with the fingers, such as buttoning the clothes, as well as formerly. Subsequently the extensors of the toes, the dorsi-flexors of the ankles, and the extensors of the wrist become paralysed, giving rise, when the limbs are not supported, to a double wrist- and double ankle-drop. The affected muscles are soft and flaccid, and undergo a progressive atrophy. This muscular atrophy, together with the unbalanced action of healthy muscles, gives rise to various abnormalities in the position and in the power of the limbs which will be now described.

*The Upper Limbs.*—The finer movements of the fingers and thumb require careful study, inasmuch as their weakness may occur before that of the extensor muscles, and constitute the first indication of the presence of neuritis. Thus, abduction and adduction of the fingers may be feebly performed, and, when the small muscles of the thumb are weak, the patient is unable to touch the tip of the little finger with the point of the thumb, except by flexing its distal phalanx ; and, when the *opponens minimi digiti* is also feeble, the point of the thumb touches the side instead of the end of the little finger. Weakness of the *opponens pollicis* allows the metacarpal bone of the thumb to be drawn backwards by the action of the long extensors, so that it lies nearly on the same plane as the other metacarpal bones. Then as the *extensor secundi internodii pollicis* becomes weak the distal phalanx of the thumb bends towards the palm ; and when the *extensor primi internodii pollicis* is affected the basal phalanx is also bent, while weakness of the *extensor ossis metacarpi* is betrayed by approximation of the metacarpal bone of the thumb to that of the index finger. When the extensors of the wrist become weak the patient cannot perform certain movements, such as grasping an object, without the wrist becoming flexed, owing to the preponderating action of

the flexor muscles. Similarly, in buttoning or unbuttoning the clothes the prominence of the curve of the flexed wrist and the fumbling of the feeble fingers are very conspicuous features. Before the extensor muscles of the fingers are completely paralysed their stretching by the flexion of the hand on the forearm causes extension of the first phalanges; the distal, however, are flexed by the long flexor. When the extensor muscles of the wrists and fingers are completely paralysed, and the patient is asked to raise his hands, the wrists are strongly flexed; while owing to the action of the interossei and lumbricales the fingers are slightly flexed at their metacarpo-phalangeal, but extended at the phalangeal joints. The attitude then frequently resembles that produced by active muscular spasm, as in tetany. As regards the upper arm the triceps is usually more paralysed than the biceps or supinator longus; hence the elbows are bent, and, owing to the necessary stretching of the shortened flexors, cannot be fully extended by passive movements without causing pain.

The progressive atrophy also contributes to the deformity of the limbs. The thenar and hypothenar eminences are flattened, and deep grooves appear on the back of the hand between the metacarpal bones, the space between the metacarpal bones of the thumb and index finger being especially hollow. The back of the forearm becomes flattened and the ulnar border loses its roundness; but the radial border usually retains its natural curve, because the supinator longus is comparatively spared, and often escapes altogether. The biceps and deltoid are also often but little affected; the triceps, however, is usually much wasted. In other cases the deltoid, biceps, and supinator longus become weak and wasted.

The Lower Limbs.—Restriction of movement is not always due to paralysis; it may depend on great tenderness of the soles and of the leg muscles. But sooner or later paralysis sets in, and is usually first declared by the patient's inability to raise the toes from the ground in walking. When the foot is unsupported, its anterior part falls down, forming an obtuse angle with the axis of the leg, instead of a right angle, as in health. In the first degree of paralysis, in addition to dropping of the feet, the toes are hyper-extended at the metatarso-phalangeal and flexed at the phalangeal joints, with the exception of the big toes, which are hyper-extended at both joints. This hyper-extension of the big toes is a characteristic feature of the early stages of neuritis; and when, as sometimes happens, it is associated with exaggeration of the knee-jerk and of the plantar reflex, the case might easily be mistaken for one of spastic paralysis due to disease of the lateral columns of the cord. In the second degree of paralysis the terminal phalanx of the big toe becomes flexed. In the third degree the whole of the big toe is bent down towards the sole, but the other toes still remain over-extended at the metacarpo-phalangeal joints. But in the fourth degree of paralysis these also become bent, and the whole fore part of the foot hangs loose and curved towards the sole; this tends to increase the concavity of the foot, although when it is placed on the ground it appears to be flatter than normal. In old-standing cases, in which the flexors of the toes and the

muscles of the sole have undergone adaptive shortening, the concavity of the foot is persistently maintained; and during the stage of recovery from paralysis the patient may be unable to bring his heels to the ground.

In addition to the muscles on the anterior aspect of the legs, the calf muscles also frequently become affected; and in advanced cases all the muscles below the knee are so wasted that anteriorly the skin appears to lie almost on the bones, while posteriorly the calves are represented by loose bags of skin. Frequently the thigh and pelvic muscles become affected, the extensors more than the flexors; and when this occurs to any serious degree the patient becomes bedridden. Then the anterior aspect of the thigh is much wasted, and the gluteal regions are flattened, soft, and pendulous; the gluteal folds feeling as if composed of little more than layers of skin. In such a case the hips and knees are flexed to about a right angle, while the ankles are hyper-extended, the anterior parts of the feet being strongly eurved towards the soles; the outer lateral surface of one limb rests on the bed with the other limb lying upon it.

The peculiar gait, seen in all marked cases of alcoholic paralysis, depends chiefly upon the flatness of the feet and the weakness of the anterior muscles of the legs. Thus, when the heel of the foot to be advanced is raised the toes drop, and are only prevented from trailing along the ground by an unusual degree of flexion of the knee and hip. The undue elevation of the knee at each step makes the gait resemble that of a high-stepping horse; and the drop of the fore part of the foot unduly exposes the sole to the view of an observer standing behind the patient.

**Muscles of the Trunk.**—In some cases the muscles of the back and abdomen are affected, and in rare cases those of the neck also. When the lumbar muscles are feeble the hollowing of the back is deepened; and if the glutei also are paralysed the patient has difficulty in rising from a chair or from the ground; in attempting to do so his attitudes closely resemble those seen in pseudo-hypertrophic paralysis. Feebleness of the abdominal muscles impairs the power of expelling the contents of the rectum and bladder, weakens the force of sudden expiratory acts such as coughing and sneezing, and takes away the patient's power of raising himself from the recumbent position. When the muscles of the neck become paralysed the patient is unable to raise his head, or even to move it on the pillow.

The further advance of the disease is indicated by implication of the muscles of respiration. The diaphragm is first attacked, its paralysis being indicated mainly by the drawing in of the epigastrium during inspiration, and by overaction of the lower intercostal muscles. When the intercostals become feeble, the patient complains of a tightness across the chest, and expansion of the chest is feeble or lost; whereas its elevation is carried on by the violent action of the extraneous muscles of respiration.



**Muscles of the Face.**—Decided paralysis of the facial muscles rarely occurs in alcoholic paralysis, but slight feebleness is not uncommon. This feebleness is shewn—(i.) by a loss of expression, the lines which give character to the face being little marked or even obliterated; (ii.) by a widening of the palpebral fissures, owing to weakening of the orbiculares palpebrarum and to retraction of the upper eyelids; and (iii.) by tremor of the lips in speaking, or on protrusion of the tongue.

Tremor and weakness of the tongue and lip muscles render articulation thick and indistinct; and in some cases this defective articulation, together with the want of tension about the lower facial muscles, presents a close resemblance to the facial and articulatory characteristics of general paralysis of the insane. Phonation, too, is frequently feeble and husky, and occasionally there is complete aphonia, these changes being due partly to laryngeal congestion and partly to weakness of the vocal cords.

**Muscles of the Eye.**—As a rule the muscles of the eyeball are spared; but in a few cases nystagmus, ptosis, convergent strabismus from weakness of the external recti, and even ophthalmoplegia externa have been observed. Ptosis and paralysis of the external rectus have been proved to depend on degenerative changes in the third and sixth nerves, but in cases of ophthalmoplegia there is usually a lesion of the nuclei. The pupils, if altered in size, are usually somewhat dilated. As a rule, they contract to light and accommodation; occasionally, according to some writers (Épéron and Raimann), the Argyll Robertson phenomenon is present. Raimann found some muscular disturbance of the eyes—unequal pupils, the Argyll Robertson phenomenon, or paralysis of some of the external muscles—in about 30 per cent of a large number of cases of alcoholic neuritis. Dr. L. Williams believes that nystagmus is not uncommon.

**Inco-ordination of Movement.**—True ataxia occurs very rarely in multiple neuritis. In the large majority of cases the disorders of gait and other motor defects are due to muscular weakness, and not merely to errors in the balance or equilibrium of the contractions of muscles by which a particular movement is performed. Thus, if the lower limbs are partially paralysed, the patient (his eyes being closed) can usually give accurate answers with regard to the position of his legs in bed; he can cross one knee over the other without any exaggeration of the necessary movement, and is often able to describe a circle in the air with his foot, and to stand with his feet together and his eyes shut, without any material increase of the unsteadiness due to his muscular weakness.

It is true that occasionally the gait of a patient suffering from multiple neuritis may present a superficial resemblance to that of ataxia; as, for example, when there is considerable anaesthesia of the soles of the feet. Then when the patient's eyes are closed he may walk in an uncertain oscillating fashion. In other cases, too, it may be noticed that extension of the knees in walking is performed with abnormal vigour, and presents the sudden jerky exaggerated action of ataxia; but a careful examination will shew that weakness of the flexors of the knee deter-



mines the undue action of the extensors. In neither instance is the resemblance to ataxia a close one. It must be admitted, however, that a genuine inco-ordination of movement does very rarely occur in cases in which the lesions are limited to the peripheral nerves, the posterior roots and root-zones being free from disease.

*The Bladder.*—The sphincters, as a rule, are unaffected. When psychical disorders are prominent, patients who are able to empty their bladders in a normal manner may pass their urine into the bed; or they may suffer from retention of urine and overflow-incontinence. When the patient's intelligence is unaffected, disorders of micturition have been occasionally observed; of these dysuria and retention are the commonest; paralytic incontinence, apart from the presence of spinal cord disease, is excessively rare. Dr. L. Williams states that rectal incontinence may continue long after control over the bladder has returned.

*Disorders of Reflex Action.*—Loss of the knee-jerks is one of the most valuable signs of peripheral neuritis; but it is important to remember that the knee-jerks in the early stage, and in the milder varieties of the disease, are frequently exaggerated. Thus, it is not uncommon in out-patient and in private practice to find increased knee-jerks in association with slight motor defects, slight anaesthesia, and a moderate degree of muscular hyperaesthesia; on the other hand, I have never seen a well-marked case of alcoholic paralysis in which the knee-jerks were present.

The cutaneous reflexes are usually enfeebled or abolished; but they may be present, and even increased, as when cutaneous hyperaesthesia is prominent. Sometimes the plantar reflex is lost when the cremasteric and abdominal reflexes are active. The latter indeed, as a rule, are not lost until paralysis is both profound and widely distributed.

The *electrical reactions* of the nerves and muscles vary. When there is obvious paralysis and muscular atrophy, some form of the reaction of degeneration is usually present; but in the minor degrees of paralysis, when it is of great importance to recognise the nature of the disease, the faradic and galvanic irritability of the nerves and muscles are either normal, or present such slight variations that an electrical examination can scarcely be regarded as of much diagnostic value.

*Changes in the Colour, Moisture, and Temperature of the Extremities.*—As already mentioned, subjective feelings of cold or heat in the extremities are common premonitory symptoms, and they may persist during the course of the disease. Sometimes they are associated with perceptible changes; thus, the fingers and toes may be white and cold, or hot, red and dry, or warm, livid and moist. The hands and feet when hanging down are often of a dark purple tint; but pale and bloodless when held above the horizontal position. In rare cases the three stages characterising Raynaud's disease have been observed in succession: namely, the stage of local syncope, in which the extremities are pale; the stage of local asphyxia, in which they are blue; and the stage of local gangrene. Ross recorded a case of this kind; the patient was suffering from numbness and tingling of the extremities, nocturnal cramps, loss of the knee-jerks,

tottering gait, and other symptoms of alcoholism; he had suffered for some time from alternating attacks of severe burning sensations in his hands and fingers, and coldness and deadness of them. When Ross saw him the palmar surfaces of the two distal phalanges of the index and middle fingers of the right hand and the dorsal surfaces of the last phalanges were of a dark livid colour; the tip of the thumb was also affected. Dark-coloured bullae had already appeared on the palmar surfaces of the affected digits, and the matrix of the nails had begun to ulcerate.

Profuse sweating is not uncommon; this may be general, or local, as on the forehead, the back of the hands and feet. The moisture, in which the feet are often bathed, is apt to be particularly offensive. At an advanced period of the disease the skin, especially on the lower limbs, becomes excessively dry and covered by scales of dried epidermis.

*Other Local Changes.*—In many cases the skin of the palms of the hands and backs of the fingers loses its wrinkles, and becomes thin, smooth, and glossy; sometimes the soles of the feet are similarly affected. The nails and hairs tend to become dry and brittle; the former may be furrowed longitudinally, and jagged and cracked at their edges. Bed-sores and perforating ulcers occur, but with extreme rarity.

*Changes in the Joints.*—Pain in the neighbourhood of the joints is not uncommon, and, in the absence of any evidence of the presence of gout or rheumatism, redness and swelling of the joints are occasionally seen; presumably as a direct result of the disease of the nerves. In chronic cases thickening of the affected joints may occur, and end in restriction of their movements. In one remarkable case, under my own care, pain over the right elbow with effusion into the joint appeared during the course of a most pronounced and characteristic case of multiple neuritis of alcoholic origin, and was followed by almost complete ankylosis. The joint affection was associated with much tenderness over the lower end of the humerus and the upper ends of the radius and ulna (*vide* also p. 113).

*Oedema* is sometimes a noticeable feature of alcoholic cases. It is usually dependent on cardiac dilatation from muscle failure; but it may occur apart from heart disease, and when no feasible explanation, other than disease of vasomotor nerves, can be given. In the latter case the oedema is usually limited to the lower extremities and to the backs of the hands; but in cases of alcoholic heart-failure the dropsy is often widespread, and erratically distributed. Caprice of localisation is indeed a peculiar feature; the walls of the chest or the lower part of the back may pit on pressure, and the scrotum be greatly swollen, when the lower limbs are comparatively free from oedema. The arms and upper part of the trunk may be involved when there is no obvious dropsy elsewhere. The face and eyelids usually escape; but in a few cases oedema of the eyelids does occur, although it is difficult to be certain whether it depends on the heart or on associated Bright's disease.

The *course* of alcoholic neuritis presents many variations. As a rule

the symptoms succeed each other gradually, and several weeks elapse before they attain their maximum intensity. Then, if the poison have been removed, there is a stationary period of one or two months, after which signs of improvement begin to shew themselves; the pain and hyperaesthesia diminish in intensity, cutaneous sensibility becomes normal, and, finally, muscular power is completely restored. Sometimes the march of the affection is very slow, and its duration much prolonged; fibro-tendinous contractions and even actual articular changes may cripple the patient for a long time; and occasionally muscular atrophy is a distinctive feature, and may persist for many years. In other cases the onset of the disease is sudden, paralysis spreads with great rapidity, and by invasion of the respiratory muscles quickly leads to a fatal issue. The description of such cases is given under "Landry's Paralysis" (p. 670).

*Complications.*—For an account of the visceral disorders and other complications of chronic alcoholism, the reader is referred to the article by Dr. Rolleston (Vol. II. Part I. p. 901). I would here merely lay stress on the frequency of psychical disorders, and of the symptoms and physical signs of cardiac failure; and on the liability of subjects of alcoholic paralysis to suffer from pulmonary tuberculosis.

The psychical disorders were divided by the late Dr. J. Ross into four stages:—(i.) The stage of exaltation, in which there are active hallucinations of sight and hearing associated with a gradual lowering of the intellectual powers. (ii.) The stage of depression, or melancholia, which is characterised by great restlessness, moroseness, mental irritability, insomnia, and horrid dreams; and frequently, too, by much morbid timidity, when the patient becomes suspicious and distrustful of his best friends. (iii.) The stage of delirium, mania, or melancholia with excitement, or of epileptiform convulsions, passing on to (iv.) the final stage of dementia. Failure of memory is one of the earliest and also one of the commonest symptoms met with in cases of alcoholic neuritis, and is usually associated with a peculiar disorder in the appreciation of time and locality. Thus, a patient may be unable to tell the day of the week, or to say whether he is in a hospital or at his own home. He cannot retain any fresh impressions in the memory; thus, if an object be shewn to him or a word be repeated to him, he is unable a few minutes later to recall the word, or to remember the object. Ultimately the memory becomes almost a complete blank; and a patient who has been lying helpless in bed for weeks may give a circumstantial account of a walk in the morning, of the public-houses he visited, and of the boon companions he met by the way. The question whether an abnormal mental condition is peculiar to alcoholic cases, or occurs also in cases of multiple neuritis from other poisons, has been much discussed since Korsakow first drew attention to the subject. He pointed out that a special form of psychosis was found in association with multiple neuritis whether produced by alcohol, or by arsenic, lead, septicaemia, enteric, or other diseases; the common factors being an altered composition of the blood, and the accumulation of poisons acting on the nervous system, peripheral or central. It has become customary



to speak of the abnormal mental condition as Korsakow's psychosis. Without entering into a discussion on the subject, I would state my belief that a characteristic polynuritic psychosis, apart from alcoholism, is rare (compare p. 203).

**ARSENICAL PARALYSIS.**—The causes of arsenical poisoning have been considered by Sir T. Oliver (Vol. II. Part I. p. 1066); from each of these, peripheral paralysis has occasionally been produced. As a rule the poison has been taken internally, very rarely it has entered the system through the skin. In the latter case the neuritis is usually local.

Thus, Conzen described the case of a girl, aged twenty-four, who was engaged in sewing and preparing furs, an occupation which necessitated the dipping of the first, second, and third fingers into an arsenical solution. In three months these fingers became numb and white, especially in cold weather, their terminal phalanges became cyanotic, and the skin smooth and shiny. The nails were grooved, thickened, and stratified, and of a dirty-grey colour. Tactile sensation was normal, but there was much hyperalgesia of the fingertips, and much sweating of both hands. There was no paralysis; the limbs were free from pain; conjunctival and digestive disturbances were absent. Conzen considered that the nerves to the affected parts were poisoned by arsenic which was taken in through the injured skin.

Internally arsenic has been taken in a single large dose or in repeated moderate or small doses. The following examples of multiple neuritis after a single large dose may be mentioned:—(1) In Raymond and Lejonne's case well-marked peripheral neuritis in the arms and legs began about ten days after the ingestion of five grams of arsenious acid; (2) a similar case recorded by Mendl; and (3) a case reported by Kron, in which a woman for headache took fifty-five pills, each containing .005 grm. of arsenious acid, in twenty hours. A few hours after this toxic dose, namely .275 grm., symptoms of peripheral neuritis began to appear.

When arsenic is taken in small doses for a long time, either accidentally or medicinally, it occasionally happens that peripheral neuritis and other symptoms of arsenical poisoning gradually appear. Thus, neuritis has occurred in patients with chorea who have taken arsenic in small doses for several weeks. It is noteworthy, however, that such cases are not common, and that many patients suffering from anaemia, chorea, or epilepsy have taken 10 to 15 minims of liquor arsenicalis daily for a long period without any signs of neuritis.

Although peripheral neuritis is not a common result of repeated small doses of arsenic alone, the result appears to be quite different when the drug is taken in combination with alcohol. This statement is largely based on experience derived during the epidemic of multiple neuritis in 1900 which was traced to arsenical beer. During the latter part of that year a great increase in the number of cases of peripheral neuritis was noticed in Manchester and the surrounding district, and especially in per-



sons who were drinking beer. Many medical men conjectured that there must be some unusual toxic substance in the beer, but Dr. Reynolds was the first to think of arsenic and to detect it in the beer. His discovery was soon confirmed by others, and the matter was thoroughly investigated. Here it must suffice to mention that (i.) in most cases the arsenic was derived from the sulphuric acid used in the preparation of glucose and invert sugar which were employed in the brewing of the cheaper kinds of beer. (ii.) The quantity of arsenic, estimated as arsenious oxide, varied in different specimens of beer from .01 to .3 grains per gallon; in a few cases the quantity was larger, even as much as one grain per gallon. An average quantity was about one-fifth or one-seventh per gallon, equivalent to 14 or 15 minims of liquor arsenicalis.

Now many of the sufferers from neuritis had taken large quantities of beer, one to two gallons daily. Others, however, had taken not more than three or four pints of beer daily, and some even a less quantity. In the former case the amount of arsenic taken would be considerable, varying from 14 to 30 or more minims of liquor arsenicalis daily. In the latter case the daily dose in terms of liquor arsenicalis would not be larger than 3 or 4 minims. Obviously when large quantities of arsenical beer are taken there is no difficulty in accounting for neuritis; it may be due either to alcohol or to arsenic. But in cases in which the quantity of beer consumed is not great, neither the amount of alcohol nor of arsenic alone can be considered adequate to produce neuritis, and it is reasonable to assume that the disease is due to the combination of the two poisons; in other words, the toxic action of beer is increased by the presence of even a small quantity of arsenic.

**Morbid Anatomy.**—The clinical history of arsenical paralysis justifies the assumption that the peripheral nerves rather than the spinal cord are implicated, but the anatomical proof of this is not yet fully established. Jarschka, in 1882, first suggested that the paralytic symptoms depend upon a multiple neuritis; and, according to Putnam, this view has been confirmed by the necropsy of a case reported in the *Canada Medical and Surgical Journal*, 1886, xiv. 716. Erlicki and Rybalken examined the nervous system in two cases of arsenical paralysis, and found disease of both the anterior horns and peripheral nerves. They believe that the degeneration of the spinal ganglion-cells, which is sometimes found in toxic cases, is due to physiological and chemical peculiarities of the blood; not to the direct effect of the poison on the nerve elements. In one case Henschen and Hildebrand found pronounced degeneration of the peripheral nerves, changes in the cells of the anterior horns, and degeneration of the columns of Goll. It has also been shewn that arsenic injected subcutaneously is capable of destroying adjacent nerves, apart from any changes in the nerve centres. The careful experiments of Vrigens, in 1881, make it probable that no part of the nervous system is exempt from the influence of the poison. Haemorrhages widely distributed in the brain and cord are sometimes found; and are supposed to be due partly to paralysis of the vasomotor nerves, and partly to changes in the

constitution of the blood and vessels. Prof. Dixon Mann has suggested that the affinity of keratin tissues for arsenic may be the cause of the initial stage of the neuritis, and may also explain the occasional presence of brain symptoms, for neuro-keratin exists in the grey and white matter of the brain, and forms a sheath round the axis-cylinder and the white substance of Schwann.

**Symptoms.**—Cases of arsenical neuritis were rare before the Manchester epidemic. Many isolated examples had been recorded, and a study of their clinical features shews that they did not differ in any important respect from those observed during the epidemic. The observation of so many cases of neuritis from arsenical beer increased our familiarity with the symptoms of arsenical poisoning, but did not greatly modify our knowledge concerning them. Hence it is unnecessary to give a separate description of the symptoms produced by arsenic alone and those by arsenical beer.

In many cases symptoms of multiple neuritis are preceded for a few days or weeks by other symptoms of arsenical poisoning, such as vomiting, diarrhoea, conjunctivitis, laryngeal and bronchial catarrh, and various skin lesions. In other cases these symptoms have been slight or absent, and a sudden or a gradual development of neuritic symptoms has been the only apparent result of the poison. Sometimes neuritis has developed not only suddenly but immediately after taking a poisonous dose of arsenic. Thus, in Kron's case paraesthesia and severe pains came on within twenty-four hours after taking a large quantity of arsenic, and these symptoms were quickly followed by almost complete and simultaneous paralysis of both arms and both legs; gastro-intestinal symptoms were absent. As a rule, however, the onset of paralysis is gradual, and is preceded by subjective symptoms of sensory disturbance, which usually are prominent and persistent. In the order of their appearance, character, and course the symptoms of arsenical are so similar to those of alcoholic neuritis that it is unnecessary to describe them in detail. It will be more profitable to give a brief summary of their points of resemblance, and then to draw attention to a few characters in which differences may be noted.

*Features common to Arsenical and Alcoholic Neuritis.*—Arsenical paralysis may be ushered in and accompanied by marked sensory disturbance. The patient complains of severe darting, tearing, and aching pains in the limbs, of numbness and tingling in the fingers and toes, and frequently of burning sensations in the soles of the feet. The spontaneous pains are often sufficiently severe to prevent sleep. Painful cramps are also present; cutaneous hyperaesthesia and tenderness on pressure of the muscular masses of the limbs are other striking features. To these irritative sensory phenomena, muscular weakness and diminution of the cutaneous sensibility in the distal portions of the limbs are quickly added.

As a rule paralysis attacks the lower before the upper extremities; occasionally, as in Kron's case, all four limbs are simultaneously affected.

Just as in alcoholic cases, the extensor muscles of the hands and feet are principally implicated, so that the patient becomes unable properly to extend his fingers, toes and wrists, and to dorsi-flex his ankles; there may be complete hand- and foot-drop. Atrophy of the weak, flaccid muscles quickly ensues, and after a time tends to be extreme. In severe cases the atrophic paralysis spreads from the distal to the proximal portions of the limbs, until finally all their muscles are more or less involved. The muscles of the trunk and in exceptional cases some of the muscles innervated by the cranial nerves become affected. In only one case of neuritis from arsenical beer did Dr. Reynolds note an affection of a cranial nerve, namely, partial anaesthesia in the territory of the left fifth nerve. Weakness of the facial muscles, however, has been recorded, and Raymond refers to disturbances of mastication and of vision. Basedow mentions the case of two children with diplopia, due to paralysis of the oculomotor muscles, after sleeping in a room the walls of which were damp and covered by a green paper containing arsenic. In a case recorded by Brouardel there was paralysis of the palate. Tachycardia is mentioned by several writers who attribute it to paralysis of the vagus.

In advanced cases of arsenical paralysis the weakness is almost universal in distribution, so that the patient lies in bed totally unable to make the slightest movement; the intercostal muscles usually escape, but the diaphragm may become paralysed, even when loss of power in the limbs is comparatively slight. The atrophied muscles often give the partial or the complete reaction of degeneration.

Tremors general or localised may be present, and spasmodic movements have also been described. Thus, Pick observed spasmodic flexion of the great toes; whilst in a remarkable case of arsenical paralysis recorded by Kovács the fingers of both hands shewed movements like those of athetosis. These movements only occurred when the limbs were at rest and ceased directly on voluntary movements. Athetoid movements of the fingers were also observed by Raymond and Lejonne in a case of acute arsenical polyneuritis.

The tendon-reactions are almost invariably lost, and the superficial reflexes are usually present. In one of my own cases the knee-jerk and the plantar reflex were both exaggerated, and it seems probable from the recorded cases that the knee-jerk is often exaggerated in the early stages of arsenical, as it is in alcoholic and other toxic palsies.

Every variety of anaesthesia has been observed, loss of sensibility to touch, to pain, and to temperature, either separately or combined. Frequently anaesthesia is associated with considerable hyperalgesia. Polyaesthesia, allocheiria, and in one case (Koehl) diminution of the stereognostic sense in the hands have been observed. The muscular sense is often affected, so much so sometimes as to constitute a true ataxia. As a rule any inco-ordination of movement can be explained or is overshadowed by muscular weakness, but occasionally it is the dominant feature of the case which then closely resembles one of tabes. Hence Dana distinguishes two types of arsenical neuritis: (a) The



ordinary mixed motor and sensory paralysis. (b) The pseudo-tabetic form in which there is no pronounced paralysis, but marked sensory troubles, and especially ataxia. The latter type is stated by Kovács to be more common in cases of chronic than acute intoxication; it was well marked in one of my own cases observed in the Manchester epidemic.

The sphincters are rarely affected except in severe cases of paralysis associated with mental disturbance to which any incontinence is usually due. In a few cases incontinence of urine occurred when the mental condition was normal, thus, Comby, Marik, and Eichhorst have each referred to temporary disturbance of the bladder. In Kron's case temporary incontinence of both urine and faeces was followed by retention of urine and obstinate constipation, lasting for several weeks. He attributes the paralysis of the detrusor urinae to a lesion of the centrifugal motor fibres to the bladder which run in the first three sacral nerves; the constipation he refers partly to weakness of the abdominal muscles and partly to disease of the motor fibres to the rectum which come from the hypogastric plexus. That constipation may be due to disease of the splanchnic nerves is suggested by a case recorded by Emminghaus. Psychical disturbances are rare and only occur in severe cases of arsenical poisoning. Hallucinations, mild delirium, stupor, and impaired memory have been observed, but when the influence of alcohol can be excluded, the mental condition is not often impaired.

The course and duration of arsenical are similar to those of alcoholic neuritis. The disease is rarely fatal; in a large number of cases recovery is complete, usually in a few months, occasionally in a few weeks, or not for two years. Sometimes recovery is only partial owing to the development and persistence of contraction of the flexor muscles, and occasionally to permanent articular changes.

*Features in Arsenical Neuritis not seen in Alcoholic Neuritis.*—These are not necessarily noticed in individual cases, but are striking when groups of cases of the two diseases are compared.

(1) Hyperaesthesia of the skin and tenderness of the muscular masses of the affected limbs are more constant and more severe in arsenical cases. It is scarcely possible to exaggerate the intensity of the hyperaesthesia sometimes present, agonising pain being caused by merely stroking the palms or the soles, or by gently squeezing a finger or a toe. Another striking peculiarity is its persistence; I have found it in cases in which recovery from paralysis was nearly complete.

(2) In many cases the joints of the fingers and toes are painful and swollen; this rarely, if ever, occurs in alcoholic cases.

(3) There is a greater tendency in arsenical than in alcoholic neuritis:—(a) to a wide distribution and rapid progress of paralysis; (b) to rapid atrophy of the muscles with fibrillar contractions; (c) to inco-ordination of movement, ataxia being rare in alcoholic cases, fairly common in arsenical cases.

(4) In characteristic alcoholic paralysis the extensors of the wrist and the dorsi-flexors of the ankle are predominantly affected, whereas arsenic



tends to pick out and attack more severely the extensors of the fingers and toes. In the arsenical hand the fingers are curled and often cannot be extended owing to contraction of the flexor muscles, the little and ring fingers being the most curled and fixed; the palmar surface often presents a close resemblance to that seen in Dupuytren's contraction.

But it must be admitted that a decision as to the alcoholic or arsenical origin of a peripheral paralysis is based less on any peculiarities in the neuritic symptoms than on the other effects of these poisons, of which, in the case of arsenic, the skin lesions are of the first importance. In the Manchester epidemic they were present in about 95 per cent of the cases. The palms and soles are often red and slightly oedematous, and may be bathed in perspiration; frequently the condition of the soles resembles that of erythromelalgia. Hyperkeratosis of these parts is a characteristic feature; in a severe case the skin is thickened and covered with thick dirty-coloured scales; in a slight case there are a few thin scales or small isolated heaps. This hyperkeratosis is slow in development and of long duration. In many cases pigmentation occurs, preceded or not by various erythematous eruptions. There is either a diffuse bronzed discoloration resembling that of Addison's disease (the mucous membranes, however, being spared), or the pigmentation is punctiform or in circumscribed spots. In a few cases herpes zoster on the body or the limbs has been found. Changes in the nails are common; they become thick and brittle, and shew transverse ridges. Sometimes the hair falls off.

**The Heart.**—Signs of cardiac failure are common in chronic alcoholism. They were present in many patients poisoned by arsenical beer, and Dr. Reynolds has no doubt "that arsenic will seriously affect the heart-muscle quite independently of alcohol."

In opposition to this view it is rare to find in records of cases of arsenical poisoning any reference to an abnormal condition of the heart.

**The Brain.**—In rare cases epileptiform convulsions have been observed. The occasional occurrence of psychical disturbance has also been noted, and Korsakow includes arsenic amongst the causes of the psychosis met with in cases of multiple neuritis. But a decided mental change, with delirium and defective memory for time and place, is strongly in favour of poisoning by alcohol.

A doubt as to the arsenical nature of a case may also be solved by an examination of the urine and the hair for arsenic. Prof. Dixon Mann obtained arsenic from the urine as late as the twenty-sixth and thirty-first day after a patient had ceased taking arsenicated beer. Should keratosis be present the scales should also be examined; in one case Prof. Dixon Mann obtained eight-tenths of a milligram of arsenic from ten grams of horny epithelial scales.

**BERIBERI.**—(*Vide* art. Vol. II. Part II. p. 615.)

**DIPHTHERITIC PARALYSIS** has been adequately described in the first volume. It is mentioned here in order to emphasise the fact that, as a rule, it conforms, in the association of sensory with motor symptoms and in their distribution, to the common type of peripheral neuritis.

Purely motor forms occur ; but they are not the rule, as might be inferred from the statements of some writers on the subject.

Of the rarer varieties of multiple neuritis, many, as those due to enteric fever (Vol. I. p. 1129), diabetes (Vol. III. p. 193), malaria (Vol. II. Part II. p. 266), carbon bisulphide (Vol. II. Part I. p. 1031), have already been referred to elsewhere. The following have not been previously described and may therefore be briefly considered.

**PUERPERAL NEURITIS.**—Leaving out of consideration paralysis due to injury of nerves during labour or to their disease from pelvic inflammation there are cases of neuritis, either multiple or limited to single nerves, which appear to depend on poisons, the result of disturbed metabolism during pregnancy or of infective or other changes in the blood occurring after labour, whether premature or at the full time. It is often impossible to determine the nature of the toxin or to exclude the influence of anaemia or of the cachexia which is so frequently associated with the puerperium. The possibility of alcohol must also be considered ; thus, Dr. Handford believes that the multiple neuritis in his cases was probably alcoholic, its onset being favoured by the lowered condition of “tissue health” attending the puerperium.

No useful distinction can be drawn between the neuritis of pregnancy and that which appears after labour, for although in the former the nerves of the lower limbs are affected before those of the upper, whilst in the latter the nerves of the arms are often first solely affected, many exceptions to this sequence are met with. It is also stated that the cranial nerves are not involved by the neuritis of pregnancy, but occasionally suffer in that occurring after delivery. Thus, optic neuritis and facial paralysis have been observed ; in a case recorded by Saenger both facial nerves were involved.

During pregnancy neuritis of every degree of intensity may occur ; it is especially apt to be severe in cases of obstinate vomiting. In its mildest form it may be represented only by pains, paraesthesia and hyperaesthesia in the limbs, paralysis being absent and recovery occurring before confinement. In other cases multiple neuritis, represented by paralysis and anaesthesia in distal portions of the limbs, is present in a typical form. These symptoms may pass away before labour, or more commonly continue and become more marked for a time after labour.

When neuritis begins after the child is born its first symptoms may be noticed within twenty-four hours or only after a few days. Möbius believes that the affection begins in, and in slight cases is limited to, the territory of the median and ulnar nerves, but Saenger found this localisation in only 11 out of 47 recorded cases.

Localised neuritis has also been observed in the nerves of the shoulder or the arms, whilst as already mentioned some of the cranial nerves are occasionally involved. In a few cases the resemblance to post-diphtheritic paralysis has been a close one. When the neuritis is widespread, mental symptoms corresponding to the psychosis described by Korsakow have occasionally been present.

As a rule the *prognosis* is favourable, and complete recovery takes place even when the development of the symptoms has been acute. Thus, in a severe case described by Eulenburg, the patient, eight days after an abortion artificially induced, became suddenly paralysed in the legs and within twenty-four hours the paralysis was complete; in forty-eight hours from the onset the arms were also completely paralysed, some of the trunk muscles were weak, and there was aphonia with paralysis of the vocal cords. Partial recovery gradually ensued, and in five months there remained an atrophic paralysis of the muscles of the forearms and legs. Occasionally there has been a fatal issue. In a case reported by Korsakow and Serbski, in addition to parenchymatous neuritis of the limb nerves, changes were found in the lumbar and sacral plexuses and in some of the cranial nerves. There was an increase of neuroglia in Goll's columns and in the lateral columns of the spinal cord. Stewart also records a severe case in which the symptoms began in the seventh month of pregnancy; in the fourth month after labour there was absolute paralysis of the legs and the distal portions of the arms. The nerve trunks and the muscles were very tender to pressure. The diaphragm became paralysed, and death occurred from pneumonia. There was an intense parenchymatous neuritis of the vagus and phrenic as well as of the nerves to the limbs. Marked vascular phenomena were also present. Changes were also found in the anterior horns and the posterior columns of the cord. Stewart considered that the peripheral nerves were affected before the cord, and that the changes in the cord were not secondary to those in the nerves, but occurred independently as a later result of the same toxin.

**SEPTICAEMIA.**—Occasionally an infected wound, often of a finger, has been followed by multiple neuritis. The interval between the advent of suppuration and the symptoms of neuritis has varied from a few weeks to months. Very rarely multiple neuritis has followed a suppuration in the lung, pleura, or bladder.

**GONORRHOEA.**—In some of the reported cases, the gonorrhoea has been complicated by cystitis, prostatitis, epididymitis, or arthritis; in others there was urethritis only. In a case reported by Raymond the onset of symptoms of multiple neuritis corresponded with a temporary suppression of the urethral discharge. This case, in the rapidity of the development of the paralysis, resembled Landry's disease; in addition to the limbs and trunk the muscles of both sides of the face were paralysed. Paralysis of the face was also observed by Wclander in a case which proved fatal from implication of the respiratory muscles; microscopically the facial nucleus and the spinal anterior horns were normal whilst the peripheral nerves were markedly degenerated.

An invasion of gonococci into the sheath of a nerve may account for neuritis of a single nerve, but it is probable that their toxins rather than the organisms themselves are responsible for the multiple variety. In this connexion it may be mentioned that Mottschanoff has shewn experimentally that gonococcic toxins will produce degenerative



changes in the spinal anterior horns as well as in the peripheral nerves.

**ERYSIPELAS.**—Multiple neuritis is a rare sequel of erysipelas, and judging from recorded cases and from one striking instance under my own care, it presents no special clinical features. It has followed erysipelas associated with wounds, or of the face in the absence of visible abrasion. Recovery after a long course is the rule; in the case under my care death occurred from respiratory paralysis.

**SYPHILITIC NEURITIS** affects mainly the cranial nerves, the spinal nerves being only occasionally implicated. The neuritis is of the interstitial form and as a rule is secondary to meningitis or other adjacent lesion. In rare cases the roots of the cranial or the spinal nerves are affected by a primary neuritis. Still more exceptional is it to meet with a multiple parenchymatous neuritis. A few cases during the secondary stage of syphilis have been recorded, and in some of them it seems probable that the neuritis was caused by the circulation of a toxin derived from the specific organism. In other cases it was difficult to exclude alcohol or the influence of mercury administered for syphilis. Thus, Strauss records a well-marked case of atrophic paralysis affecting the distal portions of the limbs and associated with sensory disturbance, which was preceded by paresis of the left 3rd, 6th, and 7th cranial nerves; the onset of the attack occurred about eight weeks after infection. The patient died from cardiac failure, due to implication of the vagus. Strauss regards his case as one of multiple neuritis, and believes that the lowering of tissue-resistance by the abuse of alcohol was the disposing, and syphilis the exciting, cause of the neuritis. A case reported by R. W. Taylor is chiefly remarkable (*a*) for the extensive affection of the cutaneous sensibility, and (*b*) for the mutilations of the fingers and toes. The first symptom was anaesthesia of the hands, and appeared about eighteen months after infection. A case similar in every respect is reported by Sorrentino. In these cases it is possible that syphilis was complicated by leprosy. Two cases of almost universal paralysis are described in detail by Dr. T. Buzzard, who believes them to be examples of peripheral neuritis caused by syphilis. Recovery in each case was absolutely complete under specific treatment.

**SENILE NEURITIS.**—Symptoms of slight neuritis are sometimes present in old persons, and degeneration of the peripheral nerves has been found at necropsies. The degeneration may be explained partly by the malnutrition of old age, and partly by an imperfect supply of blood to the nerves owing to atheroma of the arteries. Oppenheim has described 6 cases in which partial paralysis of the hands and feet, with sensory disturbance, developed very slowly and apart from pains or hyperaesthesia. Another group of cases is referred to by Stein in which pains and hyperaesthesia were conspicuous features.

**CANCER.**—Very rarely symptoms of peripheral neuritis have been observed in the course of carcinoma when all other known causes could be excluded, and the assumption has seemed probable that the etiological



factor was a toxic agent derived from the altered metabolism associated with the cancerous cachexia. In cases presenting subjective symptoms only Auché found degenerative changes in the distal branches of nerves to the limbs. The cases of cancer of the stomach recorded by Francotte and by Miura shewed the characteristic sensory and motor symptoms of general multiple neuritis; in Miura's case the diagnosis was confirmed by the subsequent histological examination.

## II. THE MOTOR TYPE

Under this heading I include cases of peripheral neuritis in which motor symptoms are dominant; sensory phenomena being either absent, or present in but slight degree. Three groups may be distinguished; namely, the spasmodic, the paralytic, and the atrophic group.

**A. The Spasmodic or Irritative Form of Neuritis, in which Spasm predominates over Paralysis.**—In considering motor phenomena it is convenient to regard the motor tract as composed of two parts, an upper and a lower segment; or, as they are now designated, central and peripheral neurons. The upper segment comprises the motor cells in the cerebral cortex and the pyramidal fibres which extend between these cortical centres and the anterior horns of the spinal cord, or the corresponding nuclei in the medulla and pons. The lower segment includes the bulbar nuclei and the anterior horns, together with the motor fibres which extend from them to the muscles. A lesion situated in any portion of the upper segment of the motor tract gives rise to a spastic paralysis—that is, to a paralysis associated with rigidity or spasm of muscular tissue. A lesion situated in any part of the lower segment gives rise to an atrophic paralysis, in which weakness is combined with relaxation and wasting of muscular tissue. We may now ask, Does muscular spasm ever occur in cases in which a lesion is limited to some portion of the lower segment? First, with regard to the *spinal nuclei*, will irritation of the motor cells in the anterior horns, and restricted to them, produce muscular spasm? Physiologists do not appear to be agreed as to the excitability of any part of the cord to direct electrical and mechanical stimuli; it is stated that the motor centres can be excited by blood heated above 40° C.; or by asphyxiated blood; or by certain poisons, such as strychnine (Landois and Stirling). The knowledge derived from a study of cord diseases does not lend any support to the opinion that spasm may be caused by a lesion limited to the anterior horns.

Secondly, as regards the *peripheral nerves*. Irritation of motor nerves, by the electric current or other stimulus, tends to produce muscular spasm. Has disease a similar effect? The answer is that spasm of the ocular muscles may result from basal meningitis, in consequence of irritation of the motor nerve-trunk; and that facial spasm may be caused by a tumour pressing on the facial nerve. With regard to the evidence

afforded by the clinical history of multiple neuritis, I would draw attention to the frequency of tremor and local spasms, and to the occasional presence of exaggerated knee-jerk in the early stages of the disease.

A fine tremor is often met with in cases of multiple neuritis. Thus, it occurs in alcoholic, in lead, and in arsenical paralysis. It is a distinguishing feature of mercurial poisoning; and in cases of poisoning, both acute and chronic, it may be followed or accompanied by symptoms of neuritis. The presence of tremor in exophthalmic goitre, and during the course of severe enteric or other specific fevers—all diseases which are due to some toxin in the blood—and the occasional association of evidence of peripheral neuritis with the tremor, are also suggestive points worthy of consideration in the pathology of tremor.

Turning now to muscular cramps and spasms, we have seen that they are common in alcoholic neuritis, and are most persistent and troublesome in the muscles of the calves of the legs. The forearms, hands, and fingers also are liable to be attacked; and the spasms are particularly apt to come on while the patient is engaged in some kind of manipulation such as writing, sewing, or playing the piano. They are often complained of by patients suffering from the slightest varieties of peripheral neuritis: thus a patient, who suffers from numbness and tingling and impairment of the special movements of the thumb and fingers, may state that his fingers feel drawn when he awakes in the morning; sometimes they are so stiff and painful that vigorous rubbing for a few minutes is necessary before they can be used. Although most prominent during the early stage of neuritis, active spasms are often present throughout its course, and may be associated with considerable paralysis. In a well-marked case of alcoholic paralysis, under my care, the position of the hands was much like that seen in tetany. The dropped wrists were the result of paralysis of the extensor muscles; but the flexion of the first phalanges of the fingers and the extension of the terminal ones were mainly caused by spasm of the interossei; this was proved by the firmness with which the fingers were pressed together, and by the resistance experienced on trying to separate them, or to extend them at the metacarpo-phalangeal joints. The fingers, too, were never completely at rest, and their quivering movements appeared to be due to intermittent contractions of the interossei.

Finally, exaggeration of the knee-jerk, suggestive of increased muscular tonus, has been met with in the early stages of diphtheritic and alcoholic paralysis—an increase which, during or even before the onset of paralysis, had given way to diminution and loss of the reflex.

Is it possible to admit the existence of an irritative form of peripheral neuritis clinically expressed by muscular spasm and by no other prominent symptom? We know that paralysis of the extremities may result from disease of the peripheral nerves. Are there cases in which a spasmodic condition of the extremities can be attributed to morbid irritation of a number of motor nerve-fibres? This question naturally suggests tetany, a disease the clinical features of which present certain

affinities with those of multiple peripheral neuritis, and is fully described in the following volume.

**B. The Paralytic Form in which Paralysis is the dominant Feature.**  
—The muscles are flaccid or wasted, while sensory and other symptoms are absent or inconspicuous. Can such a form of peripheral neuritis be admitted? Is there adequate evidence that a purely motor paralysis may depend on disease limited to peripheral nerves? To answer these questions we must consider two groups of cases:—(a) cases in which paralysis is limited to certain groups of muscles, as in lead paralysis; (b) cases in which paralysis is widespread, affecting a large number of the muscles of the limbs and often many of the trunk.

Group (a).—Lead palsy has been described elsewhere (Vol. II. Part I. p. 1049), and it is therefore only necessary to refer briefly to the two commonest varieties—the wrist-drop type and the upper-arm type—as good examples of the present group. In the former type the extensor muscles of the fingers and wrists are successively attacked by paralysis and progressive atrophy. In the latter type there is paralysis of the deltoid, biceps, brachialis anticus, and supinator longus. Now in both cases there is adequate proof that the atrophic paralysis is dependent on what appears to be a primary degenerative neuritis. Examples of localised forms of motor neuritis also occur as a result of other poisons, such as alcohol, those of influenza, of enteric, and so forth.

With regard to Group (b) the matter is not so simple. Many cases of generalised paralysis are met with in practice in which the diagnosis, especially in the early stages, is very difficult. The peripheral portions of the limbs are mainly involved; the affected muscles are flaccid, the knee-jerks are lost, and sensory phenomena are absent or inconspicuous. Have we here to deal with disease of the nerves or with disease of the anterior horns? Some of these cases are quickly fatal owing to invasion of the respiratory muscles; others survive, and the affected muscles undergo a progressive atrophy. In the former case a microscopical examination of the nervous system may be inconclusive; and even in the latter the diagnosis has sometimes to be held in reserve until the ultimate result can be foreseen; a gradual improvement and ultimate recovery pointing to multiple neuritis, a steadily increasing weakness and muscular atrophy pointing to disease of the anterior horns. That this distinction, however, does not always hold is shewn by the history of a case published by Blocq and Marinesco, in which the illness had extended over a period of twenty years. The attack was ushered in by fever and digestive derangement; there was generalised atrophic paralysis, succeeded by local recovery. Sensory symptoms were entirely absent, and the case was diagnosed as one of acute spinal paralysis. The necropsy revealed grave degeneration of the muscles and of the intramuscular nerve branches; other parts of the nerves were healthy, and senile changes only were found in the spinal cord. Blocq and Marinesco point out that multiple neuritis was indicated in the above case by the presence of psychical phenomena, diarrhoea, vomiting, oedema and vasomotor derangements.



Examples of widespread motor paralysis have also been observed in connexion with lead poisoning, diphtheria, influenza, and some other toxic causes.

The *acute cases of generalised motor paralysis* offer the greatest difficulties in diagnosis. For the most part they have been included under the names of "Landry's" or "Acute ascending paralysis." This important subject is considered in detail by Dr. F. Buzzard (p. 670).

**C. The Atrophic Form.**—The proportion between muscular atrophy and paralysis presents considerable variations in different cases of multiple neuritis. As a rule paralysis occurs first, and is succeeded by muscular atrophy, which then progresses side by side with the paralysis. In some cases paralysis is predominant, in others muscular atrophy; and the latter may progress to an extreme degree. There are indeed certain groups of cases in which wasting of muscular tissue is a primary feature, and appears sufficient to account for the degree of weakness present; and in many of them there is good evidence that the disease is a chronic form of peripheral neuritis.

Two groups may be briefly considered:—

(i.) *Localised Forms of Muscular Atrophy as Illustrated by the Aran-Duchenne Type.*—This form is characterised by paralysis and atrophy of the small muscles of the hands, namely, the interossei and those of the thenar and hypothernar eminences. Atrophy is the conspicuous feature, and accompanies rather than succeeds the loss of power. The type is named from the close resemblance the condition and attitude of the hands bear to the type of progressive muscular atrophy described by Aran and Duchenne, which is known to depend on degeneration of the ganglion-cells of the anterior horns. One of its commonest causes is lead poisoning, of which it may be the sole manifestation; but as a rule it complicates the common or wrist-drop type of paralysis. In one case of this kind, reported by Madame Dejerine-Klumpke, the spinal cord was quite healthy, but extensive changes were found in the nerves of the brachial plexus and their terminal branches.

Another cause is over-fatigue of the hand muscles from some occupation, such as sewing. A patient under my care, besides marked atrophy of the intrinsic muscles of the hands, had weakness and wasting of the flexors of the left wrist and fingers. The condition began a few years before with "prickling pains" and a feeling of numbness in the fingers, ball of the thumb, and palm of the left hand. A year later she began to suffer from the same sensations in the right hand; and she soon became unable to follow her occupation of tailoring. Some of the affected muscles were tender on pressure, and there was a slight impairment of the cutaneous sensibility of the fingers and thumb. I have seen other cases of this kind in which no cause could be discovered.

(ii.) *Generalised forms of muscular atrophy* occasionally come under observation, in which the association of pains and other sensory disorders with paralysis in the early stages of the disease suggests that they have been caused by disease in the course of the nerve-trunks and their peri-



pheral branches. Rheumatism has sometimes been the most noticeable antecedent. One variety of extensive muscular atrophy must be especially noticed; namely, the peroneal type of family amyotrophy, as described by Dr. Tooth: or, as it is sometimes called, the Charcot-Marie form of amyotrophy. This disease has been fully dealt with on p. 71. The condition described by Dejerine and Sottas as progressive hypertrophic interstitial neuritis of infancy must be mentioned here. The disease runs a slow and progressive course, and is characterised by the following symptoms:—Ataxia of the four limbs with muscular atrophy: lightning pains and very well marked disturbances of sensation with delay in its transmission; nystagmus; myosis and the Argyll Robertson phenomenon; kypho-scoliosis; marked hypertrophy and hardness of all the nerve-trunks of the limbs accessible to palpation. A necropsy in one case revealed pronounced hypertrophic sclerosis of the limb nerves, and of the anterior and posterior roots of the spinal cord; as well as a sclerosis of the posterior columns with the same distribution as in tabes.

### III. THE SENSORY TYPE

Under this heading I refer to cases in which sensory symptoms, symmetrically distributed to the extremities of the limbs, are the conspicuous features. The symmetry, the association with motor defects, and frequently also with impairment of the knee-jerks, together with the fact that complete recovery is the usual result, strongly suggest that the symptoms depend on an abnormal condition of the peripheral nerves. Such cases may be broadly divided into two classes, according to the association of weakness or of inco-ordination of movement with the sensory phenomena.

**Class A.—Sensory Symptoms are prominent, Motor Weakness is inconstant or inconspicuous.**—The slighter degrees of multiple neuritis are represented sometimes by motor defects, such as spasm or weakness of some of the special movements of the fingers and thumb, but far more commonly by various sensory disturbances. Patients often consult a physician for numbness and tingling in the fingers and toes; very often these sensations are worse at night, and may be severe enough to keep the patient awake. Sometimes they are associated with severe cramps in the extremities. On examination the cutaneous sensibility may be normal; but, when carefully investigated, it is often found impaired or lost over the tips of the fingers, or at the sides of the hands. Frequently, too, the first dorsal interosseous muscle is tender; and in many cases, especially those of alcoholic origin, there is much hyperaesthesia of a considerable number of muscles. The knee-jerks are increased, diminished, or lost. These may be the only symptoms present; or they may be accompanied by slight weakness of the movements of the digits, or even of those of the hands and feet.

When cases of slight neuritis can be traced to an obvious poison, as

alcohol or that of rheumatism, and this is removed or destroyed, then a complete recovery is the rule ; but often no cause can be discovered, and then the symptoms, although they do not increase in severity, tend to persist ; or they improve for a time and then relapse. Dyspepsia is a common antecedent. One patient told me that, after her meals, she suffered from numbness and tingling in the fingers and elbows, and from pain down the middle of the forearm ; the finger-ends also became quite cold, and the left arm red in colour. Diabetes, which rarely produces obvious multiple neuritis, often leads to symptoms of slight neuritis ; such as neuralgic pains in the legs, cramps, numbness and tingling, hyperaesthesia, and absence of knee-jerks. Paralysis, however, is rare.

I have already given a full description of the marked sensory phenomena of alcoholic neuritis which characterise the early stages of the disease, and have now to add that sometimes they are the only symptoms, even when alcohol has been taken in large quantities for a long time. The patient suffers from severe darting pains in the limbs, or aching pains in the joints ; and the case may be mistaken for one of rheumatism. The soles of the feet are so tender that to walk is agonising : their cutaneous sensibility, nevertheless, may be much diminished, the condition *anaesthesia dolorosa* being present. Muscular hyperaesthesia is extreme. There is no paralysis and no ataxia of movement. The cutaneous reflexes, and often too the knee-jerks, are much increased. Great emaciation is common, partly as a result of prolonged gastric disturbance and insomnia, but partly also as a direct result of pain. The patient's weakness, pallor, and emaciation render him particularly liable to pulmonary tuberculosis.

Gouty subjects often suffer from numbness and "tingling pains" in the finger-tips ; and in persons who inherit a strong tendency to gout these symptoms appear to be easily excited by small quantities of alcohol. Thus, Dr. Ross knew a gentleman, of gouty parentage, who experienced numbness in the finger-tips after taking a single glass of beer ; and if he persisted in taking beer at dinner for a few days, his finger-nails became dry, and cracked longitudinally. This susceptibility to certain alcoholic drinks makes it difficult to decide how far symptoms indicative of a peripheral neuritis, occurring in a gouty subject, are to be attributed to alcohol or to gout. The difficulty is illustrated by an interesting series of cases described by Dr. T. Buzzard, in which symptoms suggesting slight neuritis were present, and appeared to depend on gout ; but, as many of the patients partook pretty freely of alcohol, its direct influence could not be absolutely excluded. The symptoms in these cases were : numbness and tingling in the fingers ; acute pains radiating along a limb, often especially severe in the thumb or in one finger ; cutaneous hyperaesthesia. Dr. T. Buzzard mentions one place in particular where exquisite pain was felt on pressure ; "It lies just inside the inner and upper angle of the scapula, and the pain caused by the pressure there seems to travel down to the hand. Apparently there is neuritis of the posterior branch of a spinal nerve, the anterior branch of which enters into the

formation of the brachial plexus." These sensory phenomena are soon followed by muscular weakness and atrophy, sometimes affecting the greater portion of a limb, but as a rule limited to certain parts—such as the intrinsic muscles of the thumb, or some of the forearm muscles. Sir J. Hntehinson has drawn attention to the occurrence of attacks of neuro-retinitis in gouty subjects: in one of his cases the third cranial nerve was implicated; in another case, the left facial nerve; and another member of a gouty family suffered from neuritis of the brachial plexus.

The neuritis of leprosy is also largely sensory (Vol. II. Part II. p. 677). Cases have been published, by Chauffard and others, in which the alterations of cutaneous sensibility, so characteristic of syringomyelia, have been observed, namely, loss of sensation to pain and temperature associated with preservation of the tactile sensibility. The connexion between leprosy and syringomyelia and Morvan's disease appears in some respects to be a close one; indeed some authorities, as Zambaco, believe syringomyelia to be a variety of leprosy.

**Class B.—Sensory Symptoms are associated with Muscular Inco-ordination.**

*Neuro-tabes Peripherica.*—Under this heading two groups of cases require discussion:—

(a) Cases of ataxia in which the main lesion is disease of the posterior columns of the spinal cord—that is, ordinary tabes dorsalis—but in which changes are found in the peripheral nerves also.

(b) Cases of ataxia in which the main or only lesion is disease of the peripheral nerves.

It is now well established, from the researches of Westphal, Pierret, Pitres and Vaillard, Oppenheim and Siemerling, Dejerine, and others, that disease of the peripheral nerves, both cranial and spinal, is very frequently found in association with disease of the posterior columns in ordinary cases of tabes. Dejerine has shewn that in many cases there is a close correspondence between the distribution of anaesthesia and that of changes in the peripheral nerves; and it is highly probable also that the trophic lesions of the skin, bones, and joints depend on the process of degeneration in the peripheral nerves (*vide* p. 82). How far then is the inco-ordination in any given case due to central or to peripheral lesions?

The independence of these lesions is shewn by the combination of symmetrical cord lesions with unilateral neuritis; and by the absence of any relation between the gravity of nerve lesions and the duration, extent, or severity of the cord lesions. Thus, as Oppenheim demonstrated, considerable changes may be met with in the peripheral nerves at the onset of tabes when the cord lesions are limited; and, conversely, the peripheral nerves may be intact when sclerosis of the posterior columns, of considerable extent, has existed for a long time. The latter point is substantiated by abundant evidence; and there cannot be a reasonable doubt that, in many cases, ataxia occurs as a direct consequence of disease of the posterior root-zones.

We may now consider Group (b), and ask whether genuine ataxia ever



occurs from lesions of the peripheral nerves alone; other parts of the nervous system being healthy. At first sight such a question appears to be superfluous, because numbers of cases of ataxia in connexion with peripheral neuritis have been reported; but it is to be noted that in many of them the evidence of ataxia is not conclusive; and it is beyond question that the high-stepping gait of multiple neuritis has often been ascribed to ataxia when it was really due to paralysis of certain muscles of the legs. A little consideration of the subject suggests either that many of the published observations are inaccurate, or that there is sometimes a real difficulty in discriminating between abnormal movements which are the result of inco-ordination and those which depend on muscular weakness. To assign definite limits to the use of the term ataxia is not indeed so easy as might at first sight appear. Accurate adjustment of muscular action is necessarily impaired by weakness or by spasm of any muscle employed in a particular movement; but such imperfections of movement are not all to be included under the term "ataxia." Ataxia, or inco-ordination, implies errors in the balance of the contractions and relaxations of the groups of muscles required for a given movement, apart from alterations in their strength; and although paralysis or spasm may be found in association with ataxia, the latter, as in *tabes dorsalis*, frequently exists without the former. Nevertheless, there is sometimes a difficulty in deciding whether a defective movement is due to an alteration in the strength of certain muscles, or merely to a want of proportion between their respective actions. The difficulty referred to, however, is found mainly in the minor defects of muscular action; for, as a rule, a careful examination will enable us to decide whether certain defects in the movement of a part be due to inco-ordination, or to paralysis. Also when the two conditions are combined—as, for example, in ataxic paraplegia—the inco-ordination of movement is still recognisable, unless paralysis be profound. Hence in the earlier stages of multiple neuritis, when the muscular weakness is moderate in degree, inco-ordination of movement should, if present, be detected readily.

In the first edition of this work I recorded in detail a case of alcoholic multiple neuritis with unmistakable signs of ataxia, and similar cases have been reported by Dejerine, von Leyden, Dreschfeld and others, in which multiple neuritis was found on necropsy. Ataxic conditions have also been described in connexion with diabetes and in cases of lead and arsenic poisoning; and as following diphtheria, measles, and other acute diseases.

In most of the reported cases of ataxia occurring in connexion with peripheral neuritis, other motor and sensory symptoms were present; and this is to be expected from the constitution of the mixed peripheral nerves. Does ataxia ever occur as the only symptom in cases of multiple neuritis? That this may happen when disease is limited to certain tracts in the spinal cord we know; are there fibres in the peripheral nerves which, when picked out by disease, give rise to inco-ordination of movement, and to this alone? It is impossible to give a complete answer



to such a question at present, but we may remember that cases occur in which, whilst ataxia is pronounced, muscular weakness and sensory disorders are quite insignificant; and in which complete recovery strongly suggests peripheral rather than central lesions.

Obviously there is a difficulty in locating the lesion in some cases of ataxia. Rapid loss of the knee-jerks and of the muscular sense, in association with sensory disturbance and motor weakness, points to a peripheral rather than a central lesion; but duration appears to be the only certain test, and speedy recovery may be regarded as strongly in favour of peripheral neuritis. It is highly probable, then, from the clinical and pathological evidence adduced, that cases of ataxia, presenting no striking difference from ordinary *tabes dorsalis*, may result from disease of the distal parts of the spinal nerves, especially of the nerve-fibres which occur so abundantly in the muscle-spindles; whilst the well-known case, reported by Hughes Bennett, in which the posterior spinal roots were involved in a series of isolated sarcomatous tumours, suggests that disease limited to the proximal ends of sensory nerves may also produce ataxia. In this case it is unfortunate that the cutaneous and muscular nerve-endings escaped examination; but it is clear, as Bennett pointed out, that the primary disease did not originate there; and it seems fair to regard the case as an important pathological link between the classical lesion in the posterior root-zones and the cases of "*nervo-tabes périphérique*" described by Dejerine.

A study of the relation of ataxia to peripheral neuritis brings out two points: (i.) That ataxia is rare in multiple peripheral neuritis, even when cutaneous and muscular sensibility are profoundly affected. (ii.) That it occurs occasionally when signs of muscular weakness and of diminished cutaneous sensibility are slight or absent.

It is probable that the presence of ataxia in cases of multiple neuritis points to disease of sensory muscle-nerves and their end-organs, the muscle-spindles (which, as shewn by Dr. Batten, are diseased in *tabes*). But it is very remarkable that extreme degeneration of terminal nerve-fibres to both skin and muscle has been found in cases which did not present any signs of inco-ordination during life. It is highly important in all cases of multiple neuritis which come to necropsy that the results of histological investigation of the muscle-spindles, and of nerve-fibres to both muscle and skin, should be carefully studied in relation to any indications of ataxia during life.

#### IV. THE VASOMOTOR TYPE

In considering the subject of vasomotor symptoms in the limbs, we find that a gradual transition may be traced between the group of symptoms which belong to typical cases of multiple neuritis and the group of vasomotor phenomena which belong to Raynaud's disease (p. 140). In alcoholic paralysis, as we have seen, the fingers and toes

may become cold, dead, and white or livid; and in severe cases the extremities may become gangrenous; indeed, in a few rare cases (see p. 429), the three stages of Raynaud's disease have been observed.

The following is a brief abstract of a remarkable instance of gangrene occurring in a case of peripheral neuritis under my own care:—

A man, aged thirty-four, began, in February 1897, to suffer from dragging pains in the calf of the right leg, and subsequently from pains in the left leg. These pains continued for four or five months, and were followed by weakness of the leg. The patient, however, was able to walk until June, although he became soon tired. He took to his bed on June 22. At this time his knee-jerks were said to be exaggerated, and his speech, power of swallowing, and eyesight affected to a slight degree. No satisfactory evidence of the cause of the disease could be obtained. He was admitted to the hospital at the end of September, but in spite of treatment he gradually got worse, and died at the end of January 1898. The following is a summary of his symptoms up to December: Complete paralysis and atrophy of the muscles of the lower limbs; partial paralysis of the upper limbs. The neck and shoulder muscles not implicated, but all the muscles of the arms, forearms, and hands weak and wasted—the extensors of the wrists and fingers, and the right supinator longus, being the most affected. Cutaneous sensibility of the hands slightly impaired, that of the lower limbs not at all. Moderate cutaneous and muscular hyperaesthesia in the lower limbs; the small muscles of the hands tender when squeezed. Knee- and wrist-jerks abolished; plantar reflexes not obtainable, but cremasteric and abdominal reflexes normal. Considerable oedema of the lower extremities, but none elsewhere. The oedema diminished when the limbs were raised, and the feet, livid when dependent, became white on lifting them up from the bed. The skin of the face, trunk, and limbs had a purplish appearance; and the white streak of a scratch with the finger-nail was slowly replaced by a dusky erythema, accompanied by slight swelling. The bladder and rectum were unaffected, and the heart and other viscera healthy. The memory and other mental functions appeared to be unimpaired. From the first there was some ulcerative stomatitis, and the pharynx and epiglottis were congested. The left vocal cord was less curved, and moved much less freely than the right one. The voice became high-pitched and falsetto. There was occasionally a difficulty in expectorating, but never any real difficulty in swallowing. Early in December the lividity of the feet began to increase, and at the end of the month the toes and distal portion of the left foot were gangrenous; the three inner toes being quite black, cold, and shrivelled. On 19th January the right toes became slate-coloured, and gangrene was well marked during the last week of life.

Dr. Williamson reported as follows: “The spinal cord and the peripheral nerves were examined microscopically, and the case proved to be one of peripheral neuritis of the parenchymatous form. Degenerative changes were found in the anterior tibial nerve, in the musculo-spiral, and in the posterior interosseous nerves. The anterior tibial and the dorsalis pedis arteries were atheromatous, and a thrombus was found in the latter artery.”

As a contrast to the above case may be mentioned one described by Rakhmaninoff:—

A youth, aged seventeen, was admitted to hospital suffering from gangrene

of both feet and the lower parts of the legs. His illness dated from an attack of typhus two years previously. He became anaemic, and suffered from a feeling of coldness and numbness in the hands and feet. Lancing pains in the limbs and trunk ensued; he became liable to profuse sweats, and ultimately gangrene of the feet set in. A line of demarcation formed around the ankles, and it was deemed advisable to amputate the legs a little below the knees. The wounds healed quickly, but the patient became worse, and died of pleuropneumonia about sixteen days after the operation. Rakhmaninoff found signs of degenerative neuritis in the nerves of the upper, as well as in those of the lower limbs, and he regarded the neuritis as the main cause of the symmetrical gangrene. In the hypertrophic tissue around the nerve fasciculi he found vessels with thickened walls and narrowed or obliterated channels; but he was unable to decide whether these thickened vessels were to be regarded as secondary to the neuritis, or as primary and the direct cause of it.

In this case it is to be noted that, with the exception of pains, the ordinary symptoms of multiple neuritis were absent; and this has also been observed in other cases of symmetrical gangrene wherein degenerative neuritis was discovered after death. Peripheral neuritis has not, however, been found in all cases of Raynaud's disease, even after a careful histological examination; hence neuritis cannot be regarded as a constant or even an essential feature. Nevertheless the connexion between the two conditions is very close; and in forming an opinion regarding the pathology of Raynaud's disease the following points should be kept in mind:—

1. Degenerative neuritis has been histologically demonstrated (i.) in cases presenting well-marked motor and sensory symptoms of multiple neuritis in association with vasomotor phenomena, succeeded or not by gangrene; (ii.) in cases presenting typical symptoms of Raynaud's disease either (a) when the ordinary symptoms of multiple neuritis were present, or (b) when these were absent, as in Rakhmaninoff's case.

2. Careful histological examinations have failed to reveal changes in the peripheral nerves taken from some cases of Raynaud's disease (*vide* p. 140).

These facts tend to indicate (a) that occasionally vasomotor nerves may be picked out by disease, the symptoms resulting therefrom being identical with those of Raynaud's disease; (b) that the symptoms of Raynaud's disease do not always depend on lesions of the vasomotor nerves, but in some cases may be related to a morbid condition of vasomotor centres. In my treatise on "Peripheral Neuritis," after a full discussion of the subject now under consideration, I have stated my belief as follows: "At present it appears to me impossible to suggest a better hypothesis than that brought forward by Raynaud." He attributed the spasm of the capillary vessels to the morbid activity of vasomotor centres in the brain and cord. I argued "that the peripheral neuritis, sometimes present, must be regarded as an epiphenomenon, either as the direct result of arterial disease, as suggested by Rakhmaninoff's case, or as a nerve degeneration due either to the imperfect supply of blood, or



to changes in those central cells which preside over the nutrition of the peripheral nerve-endings." I am now inclined to regard these views as incomplete; I believe that they are applicable to many but not to all cases. In all probability the name Raynaud's disease, like Landry's paralysis, includes different groups of cases which, although presenting similar or even identical clinical features, are dissimilar in the site of the morbid action.

To put the matter in another way, I think it not unlikely that future investigations may distinguish two or three pathological varieties of Raynaud's disease: the chief lesion in one series of cases implicating vasomotor centres; the chief lesion in another series implicating vasomotor nerves; while, possibly, in a third series of cases morbid changes will be found along the whole vasomotor tract, nerve-cells as well as nerve-fibres being affected.

GENERAL PATHOLOGY OF MULTIPLE PERIPHERAL NEURITIS.—The limits of this article do not permit a complete discussion of the pathology of peripheral neuritis. The morbid changes found in the cases of paralysis from alcohol and other poisons have already been briefly summarised, and I need now only consider some of the leading features of the general pathology of the subject.

At the outset it may be stated that the existence of a group of cases characterised by the presence of certain well-defined symptoms, and by the limitation of pathological changes, wholly or chiefly, to the peripheral parts of the spinal nerves has been clearly demonstrated. In applying the name multiple peripheral neuritis to this group, it must be clearly understood that it is used in the wide sense indicated at the beginning; namely, to signify that the peripheral portions of the nerves are the chief seat of the morbid action; they are in an abnormal state, not necessarily inflammatory, while other parts of the nervous system are inconstantly, or are less specially affected.

The abnormal condition may be demonstrable on necropsy, or may conceivably be so temporary or slight as not to leave any changes visible with the highest powers of the microscope. The inclusion, therefore, of many conditions under the heading peripheral neuritis can only be justified by a consideration of their clinical analogies with other conditions in which the peripheral nerves shew definite organic change.

Perhaps the most characteristic clinical feature of multiple neuritis is symmetrical localisation of motor and sensory symptoms in the peripheral parts of the limbs. The chief motor symptom is weakness of the dorsal flexors of the feet and of the extensor muscles of the hands; whilst the sensory symptoms comprise diminution and perversion of cutaneous sensibility, together with tenderness of the nerve-trunks and muscles. Such being the case, it appears not unreasonable to suppose that symptoms other than the classical, if they present a similar distribution, may be dependent on an abnormal state of the peripheral nerves. In other words, if, in place of paralysis, muscular spasms or vascular disturbances



form the dominant features, but have the same symmetrical localisation in the extremities, is it not probable that they too may be due to peripheral neuritis? These questions have been partially discussed in connexion with Raynaud's disease. But, while admitting the importance in diagnosis of symmetrical localisation in peripheral parts, we must remember how widely the symptoms of multiple neuritis vary, both in character and distribution; and how difficult it is in some cases to decide whether the lesion be situated in the cord or in the nerves. In peripheral neuritis, instead of a symmetrical, we may have a random distribution of symptoms; instead of evidence that many nerves are affected (as we should expect from the presence of a poison in the blood) the symptoms may be confined to the territory of a plexus, or to that of a particular nerve. Dr. T. Buzzard and Brissaud have each drawn attention to partial forms of alcoholic neuritis; Lendet to a case in which the muscular branches of one ulnar nerve only were affected. Furthermore, isolated neuritis has been observed also in connexion with diabetes, influenza, and other diseases. The difficulty in diagnosis is further illustrated by cases of widespread atrophic paralysis—such as those which occur in connexion with influenza and lead poisoning, and as in the case described by Blocq and Marinesco (*vide* p. 443).

How are we, then, to explain the variations in the distribution and character of the symptoms met with in multiple neuritis? The commonest cause of the disease is admitted to be a chemical poison, which may be assumed to circulate freely in the blood, and to be conveyed to all parts of the nervous system. Its frequent action on the brain is shewn by the prevalence of psychical phenomena; the extent of its action on the spinal cord is not easy to define; and, with regard to changes found in the nerves, pathologists are not yet agreed how far such changes are primary, or how far they are secondary to minute lesions in the cord. In other words, does the central nervous system exercise any influence on the distribution and character of the symptoms presented by peripheral neuritis; and are variations in the motor and sensory phenomena to be explained by differences in the selective action of the poison on nerve-fibres, or on the ganglionic cells which preside over their nutrition?

There are three possible ways in which a limitation of changes to the peripheral nerves may be explained:—(i.) The poison selects and attacks those parts solely or predominantly: (ii.) it primarily attacks nerve-cells; and, as a consequence, those portions of the nerve-fibres which are farthest removed from their influence undergo degeneration, namely, the peripheral: (iii.) the poison acts with equal intensity on nerve-cells and nerve-fibres; the former recover, but the latter, having been robbed of vitality for a time, have lost resisting power, and degeneration, already started, steadily progresses.

At first sight it appears reasonable to conclude that if the peripheral branches of nerves are diseased alone, the poison has singled them out for attack, and has had no affinity for nerve-trunks, cord, or brain. But

we are faced by the difficulty that occasionally a trophic change, such as muscular atrophy, is met with, apart indeed from demonstrable lesions in any part of the nervous system, but where there are reasons for attributing it to central disturbance. Two instances of this are particularly suggestive—arthritic muscular atrophy, and the atrophy which in some few cases affects hemiplegic limbs.

The occurrence of muscular atrophy in hemiplegia, and sometimes (as in a case recorded by Babinski) when no spinal or neuritic changes can be discovered, suggests that the cerebral cortex may play a part in the dispensation of trophic lesions. This is also indicated by the occurrence of trophic lesions in limbs affected by hysterical paralysis; and, further, by such cases as those related by Bristowe under the heading of hysterical peripheral neuritis; and again by cases (which I have seen) in which symptoms of peripheral neuritis were manifested shortly after severe blows on the head.

With regard to arthritic muscular atrophy the evidence is against neuritis, and is in favour of the hypothesis of Charcot, namely, that the nutrition of the motor cells of the cord is deranged in a reflex manner, morbid impulses being conveyed to them from the joint nerves; and that their derangement or torpor determines the alterations in the muscles. That the process is reflex has indeed been demonstrated by Raymond, who found that a previous division of the posterior spinal roots prevented the wasting of the muscles (*vide* p. 110).

Again, in all probability, slight changes in the anterior horns will be constantly found when the histology is reinvestigated by modern methods; then it has been shewn that an experimental lesion of the posterior roots will occasionally lead to wasting of some of the cells in the anterior horns. This is an indication that the vitality of motor cells depends to some extent on the integrity of sensory fibres, and is one of the links in a further conception of the pathology of the nervous system which new histological methods are daily bringing to light. The method of Nissl, especially, has added to our knowledge of the anatomy of the nerve-cell, and has demonstrated slight pathological changes hitherto undetected. Hence it is necessary to wait for the further information to be expected from the use of these methods before we can clearly understand the relations between central and peripheral disease. It is true that before Nissl's method came into use changes in nerve-cells were found in many cases of peripheral neuritis. Duménil, forty-five years ago, in one of the cases already mentioned, found disseminated lesions in the spinal grey matter and a rarefaction of the cells of the anterior horns. Degenerative changes in these cells have also been described by von Monakow, Oeller, Oppenheim, and other observers, in cases of peripheral neuritis from lead, alcohol, and arsenic; but they were very inconstant, and the partisans of a central hypothesis for polyneuritis were obliged to fall back on supposed dynamic changes in nerve-cells. Nissl's method of staining the cells, introduced in 1885, opened up a new field of inquiry (*vide* p. 221). The researches of

Marinesco, Ballet and Dutil, thus rendered possible, have proved conclusively that minute changes in nerve-cells are very common in cases of neuritis, and that many of them are secondary to it. They shew that though nerve-fibres depend for their vitality on nerve-cells the condition of the cells is influenced by that of the fibres; not only may central changes lead to peripheral lesions, but the latter may also in turn initiate lesions in nerve centres. But although it is anatomically correct to regard the neuron and its axis-cylinder as one body rather than as two distinct bodies artificially linked together, and although it is difficult to exclude central influences from the explanation of the phenomena of peripheral neuritis, it will be granted that a predominance of pathological changes in peripheral nerves is evidence that they have been specially selected by a particular poison; now, if this be admitted, it is logical to infer that cases exist in which these parts are attacked alone, the neurons themselves presenting no affinity for the particular poison. This inference is proved to be correct by a case reported by Dejerine.

The view that nerves alone may be picked out by certain poisons receives further support from the frequent implication of sensory fibres in peripheral neuritis; for it seems more reasonable to believe that a poison will attack two adjacent structures, such as the motor and sensory fibres in a peripheral nerve, than two widely separated organs, such as the anterior horns and the ganglia on the posterior roots which preside over the functions of the sensory and motor fibres. From a clinical standpoint the differences between affections of the nerve-fibres and nerve-cells are usually well marked; but this is not always the case, as has already been indicated in connexion with acute affections of the neuron, as exemplified by cases grouped under the title Landry's disease. When sensory phenomena are well marked, as in Landry's own case, there can be little doubt that the disease is acute multiple neuritis; but when motor phenomena are solely or predominantly present it is very difficult to say which part of the peripheral neuron is affected. In some cases motor fibres are picked out, in others motor cells; in others, again, both may be affected by a toxin in the blood. The pathological selection is probably due mainly to the kind of poison, and to its dose; but partly also to antecedent weakness of the part of the neuron which is attacked.

Further, it is to be noted that toxins act not only on nerve-cells and nerve-fibres, but also, in many cases, on the vessels supplying them. The careful investigations of Dr. Fleming shew that degenerative changes in weakened nerve-fibres are greatly expedited by local effusions depending on vascular conditions. In two cases of alcoholic neuritis he found effusions particularly well marked "around the arterioles and capillaries in the endoneurial septa, and often between the nerve-fibres and the perineurium, and separating the inner lamellae of the perineurium." The exudation is greater in one part of the nerve than in another, and acts injuriously by compressing the nerve-fibres in its neighbourhood, thus causing degenerative changes in them, not merely at the level where it occurs, but also to



a greater or less extent peripherally. The effusion was always accompanied by changes in the walls of the vessels, and these vascular changes became better marked as the nerves were traced peripherally. Dr. Fleming believes that the greater the interstitial effusion, the less the chance of subsequent recovery. Dr. Cole, however, believes that degeneration of nerve-fibres is the primary element of the neuritic process, the vascular and interstitial changes being secondary to it. He says, the more severe the degeneration, the more complete is the absence of change in the sheaths, connective tissue, and vessels. Fatty degeneration of muscular tissue, probably the result of direct toxic action on the muscles, may act as a contributory factor to the nerve degeneration, because the nerves lie in great part of their course in the midst of a large mass of degenerating muscle, and hence are bathed in lymph loaded with deleterious products. According to Dr. Cole certain nerve-fibres are picked out by a particular poison not on account of any qualities they possess as nerve-fibres, but because their axis-cylinders are parts of specially susceptible neurons which are subjected over the whole extent of their cell-bodies and processes to the all-pervading influence of a poison in the blood, and that the changes in the nerve-cells are not the mere result of antecedent damage of nerve-fibres. He points out that the cells of the posterior ganglia shew changes of a similar type to that in the anterior cornual cells, and that there is an extensive acute degeneration of their central prolongations in the posterior columns of the cord, the exogenous fibres from the posterior roots being almost exclusively affected. The central and peripheral fibre-degenerations are similar manifestations of a single disorder of the whole sensory neurons. Degeneration of the posterior columns is an almost constant feature in polyneuritis, and in its distribution approximates closely to that of tabes. As regards the cortical neurons, Dr. Cole says that the Betz and other large pyramidal cells shew the same type of change as that seen in the spinal cells. "With this there is diffuse, bilaterally symmetrical degeneration of many of their related fibres in the pyramidal tracts" and also of the fibres in the anterior limbs of the internal capsule. This combination of cell-changes with fibre-degeneration is identical with that seen in the peripheral neurons. In some cases the cortical neurons are the more vulnerable, in others the peripheral. "The selective action of the toxic agent is clearly modified by differences of resistance of the various neuron-systems depending largely on hereditary and developmental factors, and the occupation and habits of the patients." There can be no doubt that Dr. Cole is correct in his view regarding the complex etiology of the polyneuritic and psychical disorders of chronic alcoholism. The manifestations of these affections have "the characters of a severe general disease of the nature of a toxæmia depending probably on an auto-intoxication from disordered metabolism." They only result indirectly from the alcoholism, and require the co-operation of various other causes, such as shock, injury, chill, pneumonia, or tuberculosis (*vide* also p. 228).

In conclusion, some of the main pathological features of peripheral neuritis may be summarised as follows :—(i.) The chief cause is a chemical



poison. (ii.) The poison affects all parts of the nervous system, though to a very unequal degree in different cases ; partly because the nature of the poison varies, and partly because individual portions of the nervous system present varying susceptibilities in different persons. It may, indeed, be safely assumed that sometimes the peripheral nerves are solely implicated ; whilst it is probable that particular fibres—motor, sensory, or vasomotor—may be picked out by special poisons. In many cases, however, there is evidence that the brain, or cord, or both, may be attacked together with the nerves.

DIAGNOSIS.—There can be little difficulty in diagnosing a well-marked case of multiple neuritis. The symmetrical distribution of the flaccid paralysis and of the sensory disorders to the distal portions of the limbs, the tenderness of the muscles and nerves, and the freedom of the bladder and rectum from disturbance of their functions are characteristic features. The chief difficulties in diagnosis are met with (1) in the early stages of the affection, (2) in acute cases of rapidly generalised paralysis, (3) when ataxia is a prominent symptom, and (4) when sensory symptoms are slight or absent.

(1) The pains of the initial stage may be mistaken for those of rheumatism or neuralgia. Rheumatic pains are related to the joints rather than to the muscles or the nerves, and are not usually associated with numbness and tingling in the hands or feet as are the pains of neuritis. The bilateral symmetry of the pains and numbness is a distinction from neuralgia, which is a unilateral disorder. Impairment of voluntary movement may be combined with the limb pains, but this is not necessarily due to paralysis ; it may depend on myositis or other disease of muscular tissue. In polymyositis we should expect hardening and contraction rather than flaccidity of the muscles ; and implication of a large number of muscles, those of the neck and back being affected as well as those of the limbs, together with an absence of any signs of real paralysis. But even when definite muscular weakness accompanies a symmetrical distribution of pain and paraesthesia, the diagnosis of neuritis may be uncertain for a time. Recovery, although an important element in the differential diagnosis between disease of the nerves and of the spinal cord, cannot be relied on with certainty. There can be no doubt that occasionally serious lesions of the spinal cord, such as myelitis, pass away entirely.

In the early stage of multiple neuritis the knee-jerk may be abnormally brisk, but the exaggeration soon gives place to diminution and loss, nor is it ever associated with ankle-clonus or Babinski's sign. Hence any suspicion of a commencing spastic paraplegia is soon dispelled. Moreover, exaggeration of the knee-jerk in the irritative stage of neuritis is associated usually with the characteristic sensory symptoms of that period, and sometimes also with loss of the tendo-Achillis jerk, for this reflex may disappear before the knee-jerk. Slight weakness of the legs with loss of the knee-jerk occurs in cases of commencing myelitis in the lumbar region of the cord, but then as a rule there is also weakness of

the sphincter vesicae, whilst the distribution of any anaesthesia present is different to that in peripheral neuritis.

(2) For the diagnosis of acute rapidly progressive cases of paralysis, which is often very difficult, see article on Landry's paralysis (p. 670).

(3) Ataxia, as already stated, is rare in multiple neuritis; occasionally it is prominent, and if associated with sensory symptoms and loss of the knee-jerks whilst muscular weakness is inconspicuous, it may be difficult or impossible, at least for a time, to exclude tabes. This is not surprising in the light of our knowledge that the exogenous fibres in the cord from the posterior roots are often diseased in multiple neuritis, and the peripheral nerves in tabes. In fact, inco-ordination of movement may result from a lesion in any part of the muscle-sense tract, whether it be the fibres from the muscle-spindles or those from the posterior roots which are continued up the cord. A priori, indeed, it might have been thought that ataxia would be common in multiple neuritis—the distal portions of the muscle-sense tract being presumably affected along with other peripheral nerve-fibres—rather than rare.

In true tabes the symptoms to be relied on are:—The Argyll Robertson pupil, girdle sensations, deranged micturition, and, if present, optic atrophy. These symptoms do not occur in multiple neuritis, though pallor of the temporal halves of the discs is sometimes present in alcoholic neuritis. The pains of tabes are sharper and more darting in character than those of neuritis. In favour of neuritis also would be much tenderness of the muscles and nerves, and a relatively rapid onset of ataxia after sensations of numbness and tingling in the extremities. Gastric crises are common in tabes, rare in neuritis, and then do not occur in a typical form. In tabes they may be separated by distinct intervals of complete freedom; in neuritis, pain and vomiting are more closely related to some temporary disorder of the stomach. In one of my cases of multiple neuritis gastralgic attacks ceased when sugar, which had been taken immoderately, was prohibited. The superficial abdominal reflexes are frequently much exaggerated in early tabes; they are normal or diminished in multiple neuritis. Then thoracic bands of partial anaesthesia are found in tabes but not in neuritis. In doubtful cases the return of the knee-jerk—previously lost—and a partial or complete recovery from other symptoms would point to neuritis rather than tabes. For although in tabes marked ataxia may subside and other symptoms become arrested, knee-jerks once lost rarely if ever return. Lymphocytosis of the cerebrospinal fluid is present in at least 85 per cent of cases of tabes; it is not found in cases of peripheral neuritis.

(4) Leaving out of consideration the acute forms of extensive paralysis, the diagnosis of which is discussed elsewhere (p. 670), there are cases of multiple neuritis which follow the usual course with the exception that sensory symptoms are slight or absent. There are no pains, no hyperaesthesia and no anaesthesia, whilst an atrophic paralysis of the usual distribution affects the limbs. The question arises, does the paralysis depend on a lesion of the anterior horns in the cervical and

lumbar enlargements or on a neuritis limited to the motor fibres of the peripheral nerves? In the former case there is no history of the usual causes of multiple neuritis, and there are none of the mental symptoms which are so frequently met with in alcoholic neuritis. The development and distribution of the paralysis are different in the two cases. Then some of the cranial nerves, as the oculomotor, the facial, or the vagus may be affected in multiple neuritis, but not in acute poliomyelitis. In favour of neuritis also would be the presence of ataxia, however slight. Frequently too in these cases of motor neuritis the tuning-fork test may reveal loss of the vibrating sensation, a sure indication that some sensory fibres are involved.

A type of paralysis has been described by Dr. S. Barnes, and called "toxic degeneration of the lower neurons," which resembles multiple neuritis, but is associated with marked atrophy of the hand muscles, and with only slight sensory symptoms. In some respects the condition resembles that of progressive muscular atrophy, but the etiology is different, and there is a constant tendency to improvement. In one case Dr. Barnes found degenerative changes both in the peripheral nerves of the arms and in the nerve-cells of the spinal anterior horns.

PROGNOSIS.—In an ordinary case of multiple neuritis, when the patient is removed from the influence of the exciting cause and is placed under favourable conditions, recovery—partial or complete—may be expected, and even when paralysis is more extensive than usual, implicating the proximal as well as the distal muscles of the limbs, and possibly also the diaphragm, a hopeful prognosis is frequently justified. I have seen several cases of almost universal paralysis in which complete recovery ultimately ensued; one case occurred as a result of lead poisoning. The patient on admission to hospital was quite helpless, both arms and both legs were completely paralysed, and the trunk muscles, the diaphragm, and the lower intercostal muscles were also implicated. After lying in bed for several months, unable to move his body or limbs, improvement slowly set in, and in a year and a half's time the muscles of the wrists and fingers were the only ones to shew diminished power. The duration of these severe cases is often very long, and some of the muscles, such as those of the hand and the peronei, may remain permanently weak and wasted. Contraction of the limbs and articular changes are also occasionally persistent. When psychical disturbance is severe and prolonged, permanent mental weakness must be anticipated.

In estimating the danger to life attention must be paid to the general condition of the patient, the rapidity with which paralysis has spread, and the nature and severity of any complications that may be present. In alcoholic cases the vitality of the patient is often much lowered, and the tissues may offer a feeble resistance, to the attacks of tubercle bacilli, pneumococci, or other morbid agents. If the patient's strength is still further reduced by gastro-intestinal disturbance or bronchitis, his condition may speedily become dangerous.

The subjects of alcoholic neuritis are peculiarly liable to pulmonary



tuberculosis, which would be furthered by any defect in the respiratory movements, such as paralysis of the diaphragm, especially when combined with weakness of the lower intercostal muscles. Impaired action of the heart as a result either of weakness of its muscle or of disease of the vagus is another serious complication frequently met with in cases of alcoholic neuritis. Cardiac muscle failure is a common cause of death. In all cases of multiple neuritis the risk to life is increased by the presence of any indications that the spinal cord is involved.

The prognosis is also unfavourable when the development and spread of paralysis are rapid, whether this occurs from the first, or only after the existence for a time of slight symptoms of neuritis. In such acute cases, for which often no adequate cause can be discovered, the mortality is high owing to the frequency with which the paralysis spreads to the respiratory muscles, and the tendency to pneumonia.

**THE TREATMENT OF PERIPHERAL NEURITIS.**—The first essential in dealing with any case of peripheral neuritis is to find out the cause, and to remove it, or to stop its action, as soon as possible. The cause, as we have seen, is nearly always some poison; and, if the patient be withdrawn from its influence and placed under favourable conditions, complete recovery is the rule. There is abundant proof that muscles extremely atrophied as a result of neuritis may completely regain their normal bulk, strength, and electrical reactions. Hence it is clear that nerve-fibres profoundly degenerated may be entirely reformed; new axis-cylinders may develop, and become covered with myelin; and ultimately a new set of nerve-fibres may convey healthy impulses to healthy muscles.

In cases due to alcohol the patient should be deprived at once of alcoholic drink in any form; even in old, broken-down toppers the deprivation is rarely attended with danger, if suitable nourishment be administered and careful attention be given to the digestive organs. To provide against deception on the part of the patient, and to ensure the complete withdrawal of alcohol, it is often necessary to remove the patient from the care of his friends, and to place him in the charge of trained and trustworthy nurses.

In all except the slightest cases rest in bed is advisable. The patient is thus protected from exposure to cold, the pernicious effects of movement are reduced to a minimum, and local treatment can be carried out more readily and satisfactorily.

In the acute stage the suffering of some patients is extreme; and it is of the utmost importance to relieve this as promptly and effectively as possible. The severest cases require a water-bed; this not only relieves pain better than an ordinary bed, but also gives more support to a weak patient, and thus lessens the danger to life arising from a feeble, dilated heart or paralysed respiratory muscles.

In feeding the patient, or in attending to his evacuations, the nurse should exercise the greatest care and gentleness: so that all unnecessary movements on the part of the patient may be avoided. On no account must she attempt to massage the limbs. For the relief of tender nerves



and muscles there is nothing better than warm fomentations. It is best to apply them intermittently ; a warm fomentation may be put on the painful part for half an hour, and the application repeated every four hours ; a layer of hot cotton-wool taking its place in the intervals. Mills recommends rapidly alternating applications of very hot and very cold water ; "a large sponge or soft towel is dipped in very hot and another in very cold water, and one is made to follow the other rapidly up and down the limb." Occasional vapour-baths often afford the patient great comfort ; but they should not be used when the action of the heart is much impaired. As regards drugs ; in the early stages of multiple neuritis, salicylate of sodium and iodide of potassium, either alone or in combination, appear to be of service ; Mills speaks highly, too, of oil of gaultheria. Neuralgic pains may also be relieved by the administration of antipyrin, phenacetin, aspirin, or exalgin ; but when the suffering is very great the hypodermic injection of morphine becomes necessary.

The drugs mentioned are of value in all forms of peripheral neuritis, but special treatment is called for in particular cases. Thus, quinine must be given when paralysis is due to malarial poisoning ; mercury and iodide of potassium in syphilitic cases ; when the neuritis depends on anaemia or on septicaemia, perchloride of iron in large doses deserves a trial. The weak, dilated heart of alcoholism requires digitalis and strychnine, to which small doses of cocaine may often be added to lessen the craving for stimulants.

But of far greater importance than drugs is the regular and careful administration of nourishment, in the form of boiled milk, beef-tea, beef extracts, soups, and broths. Benger's food or peptonised gruel may be required ; and when vomiting is a prominent symptom nutrient enemata should be administered.

Complete rest in bed in a well-ventilated room, careful feeding, and exposure to sunlight are the essential points in the treatment of the early stages of multiple neuritis.

When the acute symptoms have subsided, recourse may be had to massage, electricity, and tonic treatment. In the acute stage massage would be unendurable, and no doubt hurtful ; but its application should not be delayed too long. It may be employed as soon as extreme pain and tenderness have disappeared. At first massage should be employed in the gentlest manner, and only for short periods of time ; but as soon as the patient stands it well it ought to be regularly and vigorously applied. The patient should also be encouraged to make voluntary movement against resistance ; and other modes of Swedish exercises can be employed with advantage. Inco-ordination of movement is best treated by Frenkel's method, the essential feature of which is to submit the affected parts to a series of graduated and systematic exercises. By these means the nutrition and strength of the muscles are improved, while any tendency to contractures is overcome. Moreover, the patient's capacity for assimilation of food is thus steadily increased. The restoration of the degenerated nerves and muscles may also be aided by the daily

application of electricity. The constant current is the most useful in stimulating the nutrition of the affected muscles. Large electrodes are desirable in order that as much muscular tissue as possible may be reached by the current. As soon as the muscles respond to a weak faradic current this form of electricity may also be employed with advantage. A daily warm bath, followed by vigorous friction to the skin, is of value, whilst tonics and cod-liver oil often prove of great service.

When should the patient be allowed to get up? Not until pain and tenderness have subsided, and there is evidence that the process of repair has become established.

From first to last abundant fresh air and sunlight are of the greatest importance; and as soon as the patient is able to take outdoor exercise a change of air is often advisable; in many cases, however, it will be some time before local massage can be entirely dispensed with.

As to the efficacy of drugs in the elimination of poisons from the system fresh investigations are needed. The experiments made by Prof. Dixon Mann shew that iodide of potassium has no appreciable influence on the elimination of lead. He made a systematic examination, extending over several months, of the urine and faeces taken from cases of lead poisoning, and found that no medicinal treatment had any effect on the rate of elimination of this poison. A certain proportion of lead forms definite combinations with organic matter, and may remain in the system for an indefinite time; but a small proportion undergoes progressive elimination independently of any treatment. Professor Mann believes, however, that warm baths and general massage do contribute to a slight extent to increase the rate of normal elimination.

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Full bibliographies of multiple neuritis will be found (1) in the *Treatise on Peripheral Neuritis* by Ross and Bury, and (2) in the large volume on *Neuritis und Polyneuritis* by Remak and Flatau. The former work contains an analysis (by Ross) of a large number of cases of Landry's paralysis, and is rich in detailed records of original cases of multiple neuritis observed by the authors. The latter work is the most complete account of the subject in any language; the rarest varieties of neuritis are adequately considered, and its literature up to 1900 is given in full. It seems unnecessary to repeat the list of articles mentioned in those books. The following references comprise the more important contributions to the subject since the year 1900, together with a few others not included in the above volumes.

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J. S. B.

## HERPES ZOSTER

SYNONYMS.—*Shingles*; *Zona*.

(INCLUDING H. ZOSTER OPHTHALMICUS)

By HENRY HEAD, M.D., F.R.S.

THE name herpes was used by the older physicians for any creeping eruption; even lupus was once spoken of as "herpes excedens." But since the time of Willan the generic name of herpes has been confined to acute eruptions characterised by the presence of groups of vesicles on an erythematous base. Even so this group contains herpes iris, which bears no pathological or clinical relation to herpes zoster, herpes febrilis (or labialis), and herpes praeputialis. In the present day the generic name herpes and the adjective "herpetic" have become more and more confined to the eruptions of H. zoster, H. labialis, and H. praeputialis.

Yet there has never been any confusion with regard to H. zoster, or zona, since the disease was first described. For this name is confined solely to an acute vesicular eruption running round one-half of the body in the form of a girdle. After more or less prodromal neuralgia, affecting definite nerve territories, groups of painful papules on an erythematous base suddenly appear. These rapidly become vesicles filled with fluid, clear at first, but later usually purulent, or even blood-stained. The vesicles usually break, forming shallow ulcers that leave more or less scarring. Each eruption follows the distribution of nerve-fibres in connexion with one, or more rarely two, posterior-root ganglia.

So far the disease and its name are both absolutely distinctive. But eruptions of an exactly similar nature occur on the limbs. In such situations the characteristic appearance of the half-girdle is lost to the uneducated eye. But for the morphologist the eruption still runs from dorsum to venter, and the name "zoster" is, therefore, morphologically

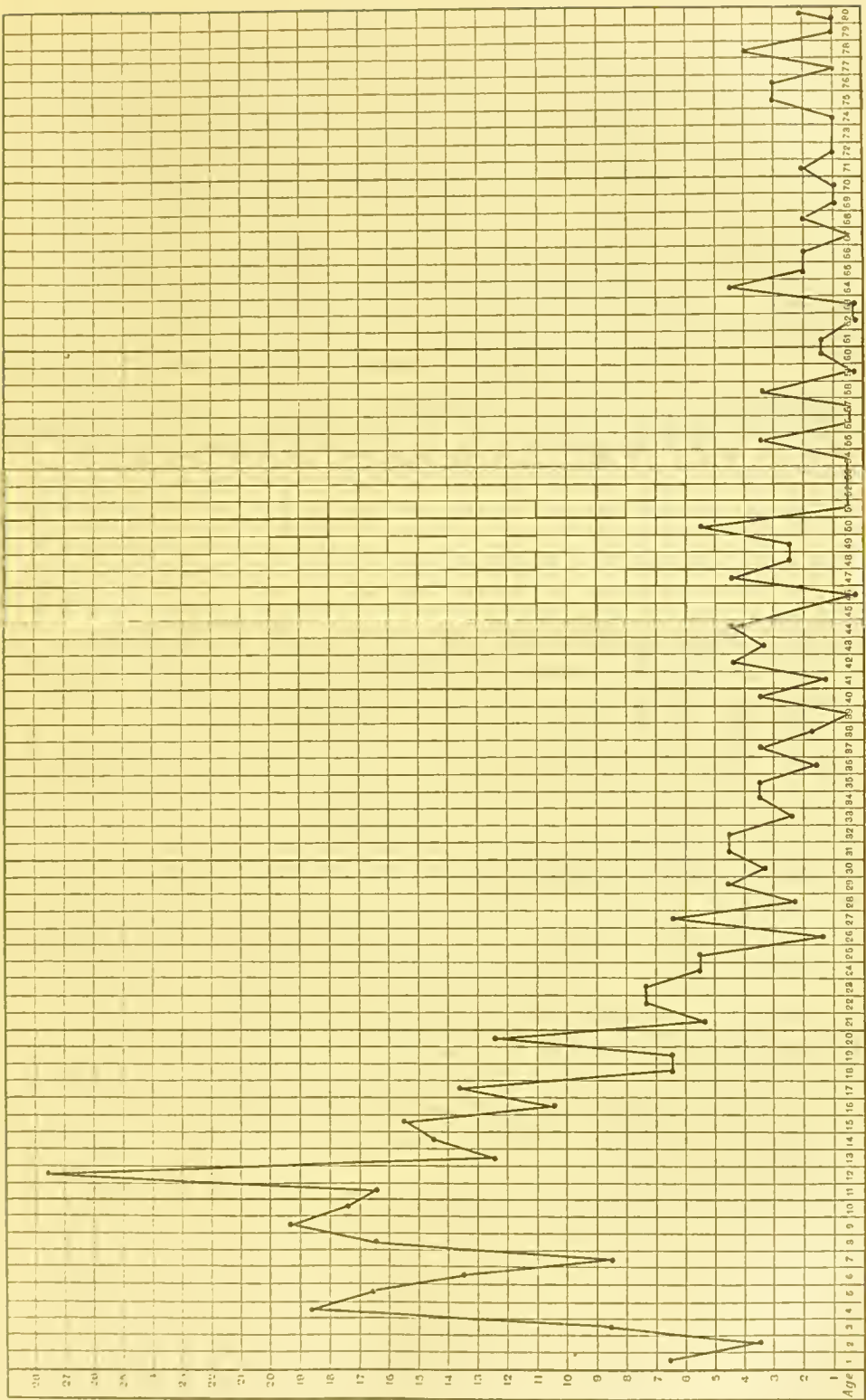


CHART 1.—To show the age-incidence of herpes zoster from 378 personally collected cases.



as correct for an eruption on the arm or leg as for one on the trunk. Again, on the scalp the eruption follows the distribution of various branches of the Gasserian ganglion, and it is only because of the peculiar structure of this ganglion that the eruption does not run from the morphological dorsum to the morphological venter. Thus *H. "brachialis," "sacralis," "collaris,"* and the like, are but useless and confusing names; and, wherever it be situated, it is better to speak of an eruption having the above well-defined course and characteristics as herpes zoster, or zona. "*H. ophthalmicus*" is a useful name for that peculiarly definite form that attacks the territory of the ophthalmic branch from the Gasserian ganglion; yet even here it is better to speak of *H. zoster ophthalmicus*.

Accuracy in nomenclature is necessary in order that there may be no confusion between herpes zoster and herpes febrilis (or labialis). The latter disease bears no relation to herpes zoster, excepting only that it is a papular eruption which becomes pustular. For (i.) it is habitually recurrent, whereas herpes zoster extremely rarely occurs twice in the same individual; (ii.) it is usually bilateral, whereas bilateral herpes zoster is of extreme rarity; (iii.) it does not follow any central nerve area, and is not associated with any changes in the central nervous system; (iv.) it may occur simultaneously with *H. zoster* in the same individual. *H. praeputialis* belongs to the same group of diseases as *H. febrilis*, and differs from zoster in the four characteristics just mentioned.

Thus this article will only treat of herpes zoster, or zona; and no eruption will be described that does not come directly within the limits of this disease.

Amongst 127,000 cases of all forms of diseases and injury that came to the receiving-room of the London Hospital in twelve months, 127 were cases of zoster (1 in 1000; or 1 in 418 of the medical cases).

**Causes.**—*Sex* is said not to have any marked influence on the disease; but out of 378 cases of which I have records, 240 were males and 138 females.

*Age.*—The most various statements are made in the textbooks with regard to the age at which *H. zoster* is most prone to occur; the differences probably arise from the comparatively small number of cases that are likely to fall to the lot of a single observer. If, however, it be permissible to generalise from my own experience, I find that out of 378 cases 283 were under the age of twenty-five; 66 between twenty-five and fifty years, and 29 over fifty years. If these cases are arranged on a chart the maximum incidence between the ages of twelve and thirteen is beautifully seen. Broadly speaking, the age at which the disease is most apt to occur lies between three and twenty, with a more particular proneness to attack between four and thirteen. Children below one year of age are not commonly subjects of this disease; but I have seen four cases under one year, the youngest of which was six months old. A case has been recorded in an infant four days old (Lomer). It is usually stated that the aged are peculiarly susceptible



to zoster, but from my 378 cases this does not appear to be so. The notion has probably arisen from the extreme severity of zoster in old persons. Thus, whilst a person of middle age may have an attack of zoster of benign course, zoster in the old is always accompanied by severe pain, and necessitates medical treatment.

**Pathogeny.**—A certain number of cases of zoster bear a definite relation to some pre-existing disease in either the central or peripheral portions of the nervous system. In them the eruption is only a symptom of some such disease as myelitis, caries of the spine, or tabes. Such cases may be classed under the heading Symptomatic zoster.

But in the majority of cases zoster arises without any known cause. Cold is invoked to explain its otherwise mysterious origin, just as cold is called in to explain acute lobar pneumonia, erysipelas, and other acute infective diseases. Like the acute infective diseases (Kaposi, Rohé) zoster begins suddenly with more or less fever, and after a variable period the characteristic lesion appears. It runs a definite course, tends to occur in epidemics, and second attacks are rare. All these features point to the essentially acute and specific nature of *H. zoster*.

Thus an outbreak of *H. zoster* may arise (*a*) as a symptom of some pre-existing disease of the nervous system, or (*b*) as an acute disease, probably as specific as acute lobar pneumonia.

*Spontaneous or Acute Specific Zoster.*—A typical attack of *H. zoster* arises without any obvious peripheral or central cause, and must be considered as an acute specific disease of the nervous system analogous to acute poliomyelitis. For it starts with a prodromal period of varying length, during which, in the majority of cases, the temperature is raised. During this period the patient feels ill and has more or less pain; but it is impossible then to make a diagnosis. If a child, he is supposed to be sickening for an acute febrile disease. Suddenly, after a variable period, the rash comes on and the disease declares itself. Thus, in their onset *H. zoster* and acute poliomyelitis closely resemble one another. Moreover, the lesion is in the one case an acute inflammation in the region of the motor cells of the anterior horns, followed by more or less secondary degeneration in consequence of the destruction of these cells; in the other, an inflammation or haemorrhage into the posterior-root ganglia, also followed by secondary degeneration due to the destruction of the ganglion-cells of the posterior root. Now the cells of the posterior-root ganglion are the morphological equivalents of the large cells of the anterior horn, and thus the parallel between the two diseases is complete. The reason that zoster is commoner than poliomyelitis is probably that one who has suffered from zoster is not hampered in the struggle for existence, whilst anterior poliomyelitis materially diminishes the likelihood of the patient's survival in the struggle.

If zoster be an acute specific disease, second attacks should be uncommon, and we find, as a fact, that second attacks of spontaneous zoster are rarer than second attacks of measles. Again, it should tend

to occur more at certain periods than at others, or even in actual epidemics. This is now recognised to be the case. My records of two and a half years at the London Hospital tend also to bear out this statement; for although sporadic cases occur throughout the year, at certain seasons of the year they increase greatly in number. Throughout the years of which I have a complete record these seasons have varied; they seem to depend on atmospheric conditions of which we are as yet ignorant. Thus, in 1896, 1897, and 1898 there was an epidemic in the middle of March. In 1897 and 1898 there was an outbreak from the middle to the end of May. In 1897 a large number of cases appeared during the long drought that lasted from the end of July on to the beginning of November; and during this period of 4 months I saw 58 cases, or one-half of the cases in the year. In 1898 several cases appeared in June, and there was an outbreak from the middle of July to the end of August, during which period I saw 22 cases in a little under 6 weeks. Another outbreak occurred in the middle of October. Thus there can be little doubt that the occurrence of large numbers of cases of spontaneous zoster is associated with some atmospheric influence or conjunction of which we are as yet ignorant. When this influence is at its highest, those persons are particularly liable to be attacked in whom the resistance is weakened by some intercurrent disease. Thus, many of the children attacked had recently suffered from whooping-cough, measles, diarrhoea, or some other children's ailment. Pregnant women are also liable to attacks of zoster, and I have seen it immediately follow ovariotomy.

Pulmonary tuberculosis is also a well-marked predisposing factor, and in times of epidemic I always see several cases in which zoster has attacked patients with this disease. The distribution of the eruption does not bear any relation to the position of the pain produced by destruction of the lung; for in several such cases the area occupied by the eruption lay over parts of the body never affected by the pain of pulmonary disease.

Sir Jonathan Hutchinson first suggested that arsenic is apt to produce zoster; for he stated that patients under the influence of this drug are prone to the disease. Nielsen found 10 cases of zoster among 557 patients with psoriasis who were taking arsenic; but not one case amongst 220 that were not taking this drug. Zoster was noticed to be specially frequent and to assume an epidemic form during the outbreak of arsenical poisoning due to beer in the Midlands in 1901 (Reynolds). I have seen many cases in persons who were taking arsenic for chorea and other diseases during those periods when zoster was rife amongst those who were not taking arsenic. Thus it is probable that Sir J. Hutchinson's impression is correct. Yet in such cases arsenic is not a proximate cause of the eruption, but only a remote cause, in so far as it renders the patient more liable to attack.

Attacks of zoster are frequently attributed to mental causes, such as fear or sorrow. Such attribution seems as little proven in the case of zoster as elsewhere in medicine where it has been invoked to explain

organic disease. Mental disease, as such, does not seem to dispose to zoster; but a considerable number of the insane suffer also from some bodily ailment, so that zoster is fairly common in large asylums. General paralysis of the insane (*dementia paralytica*) undoubtedly disposes to zoster; and the majority of cases that have come under the notice of Dr. Campbell and myself in two county asylums were in patients suffering from general paralysis. We are not yet able to decide whether in such cases the zoster is symptomatic, as in the allied disease *tubes*, or whether the debilitated condition of these patients renders them peculiarly prone to attack, as they are prone to attacks of acute lobar pneumonia, colitis epidemica, and other diseases.

*Symptomatic Zoster.*—The occurrence of zoster in cerebral disease does not stand in any direct connexion with the brain lesion, but is probably due to the decreased resistance of such patients, whereby liability to attack is increased. In one such case, in which we obtained a necropsy, we could not find any obvious connexion between the brain lesion that had caused hemiplegia and the local ganglion-lesion that had produced the zoster. The lesion in the ganglion differed in no way from that seen in other cases, and the eruption occurred at a period marked by the occurrence, both outside and inside the hospital, of an increased number of cases. But I repeat that zoster is a common occurrence in general paralysis of the insane (*dementia paralytica*).

Zoster may be a direct symptom of myelitis, for the area occupied by the rash not infrequently coincides with the upper level of the anaesthesia. In some cases of myelitis the upper level of the loss of sensation is surmounted by a band of hyperalgesia representing the area of the cord undergoing destruction; and I have twice seen zoster appear within this area of hyperalgesia. In one of these cases, which I watched for nearly a year, the area that had been occupied by the zoster ultimately became the highest area occupied by the loss of sensation when the disease in the cord quieted down and became stationary. It is probable that in some of the extremely few well-authenticated cases of zoster distributed bilaterally at the same level, the appearance of the eruption may have been due to disease of the spinal cord (Bramwell).

There are also several well-authenticated cases of the appearance of zoster in caries and necrosis of the ribs (Dubler). In one of the cases examined by Dr. Campbell and myself the ganglia were invaded by multiple growths of sarcoma which had spread into the intervertebral foramina from a mass of glands on the anterior surface of the vertebral column. Again, herpes is by no means uncommon in caries of the spine; and in such cases I have always found that the area occupied by the eruption corresponded to the distribution of that posterior root which must have been affected by the fresh outbreak of acute disease. Thus, in two cases of old spinal caries the clinical symptoms of recrudescence of the vertebral disease were accompanied by zoster over that root which corresponded to the acme of the curve and the local spinal tenderness.



In tabes outbreaks of zoster are a classical symptom; but in my experience this phenomenon is rarer than the textbooks would lead us to suppose. I have seen five instances only. In no case was the eruption complete, and it did not shew that virulent intensity so frequently seen in spontaneous zoster; moreover, the eruption continued to come out over a longer period than is usual in spontaneous zoster (during eight weeks in one case), and tended to recur. In every case the eruption was situated in the territory previously occupied by intense lightning pains. The occurrence of zoster in tabes is of great theoretical interest in connexion with the changes in the posterior roots found in this disease. Epidemic cerebrospinal meningitis is frequently associated with herpetiform eruptions which may extend widely over the body. In one case under my care at least six nerve-root areas were affected in different parts of the body and limbs, and the eruption assumed all forms from acute gangrenous areas to groups of erythematous patches.

Crops of bullous eruptions are described as occurring after injury to peripheral nerves (Weir Mitchell, Charcot). It is, however, doubtful if such eruptions should be classed with zoster, for they only occur over the territory of the wounded nerve, and do not follow a central course (Head and Sherren). In Weir Mitchell's cases they occurred, with other trophic changes, within the anaesthetic area.

**Pathology.**—1. *The Structure of the Vesicle.*—A vesicle of II. zoster at its height is a unilocular cavity, with its floor consisting of naked papillae. Incomplete partitions are formed by altered epithelial cells which retain their attachment to the roof of the vesicle. The cavity is filled with swollen epithelial cells of all ages, which have lost their prickles. Together with these loosened cells are leucocytes that have emigrated from the vessels. Certain protozoon-like bodies are also visible in the vesicle (Pfeiffer); but these have been shewn to occur in vaccinia and varicella (*vide* Vol. II. Part II. p. 108), and are probably altered epithelial cells (Unna, Hartzell). The papillae beneath the vesicle are engorged with blood, and contain many wandering leucocytes. Under a scab, which consists of the whole contents of the vesicles, restitution takes place by the ingrowth of young epithelial cells from the periphery to cover the base of the vesicles (Unna).

The fine nerve-twigs in the deep layers of the corium shew definite swelling of the neurilemma, the myelinated sheath is degenerated, and the axis-cylinder shews moniliform swellings. The larger branches shew marked degenerative changes (by Marchi's method), ten days after the first onset of the eruption (Campbell and Head).

2. *Lesions in the Nervous System.*—Von Bärensprung (1862) first suggested that the lesion associated with zoster lies in the ganglion of the posterior root. He examined one case after death, and, so far as the primitive microscopical methods at his disposal permitted, proved that "three ganglia" were affected, but "one more than the others." A child of one year, suffering from tuberculosis, was affected with zoster within the area of the 7th dorsal root; at the necropsy, six weeks



later, the 6th, 7th, and 8th dorsal nerves and ganglia were found reddened or thickened, but the 7th more than any other. Microscopical examination shewed that the ganglion contained a fine brown mass, apparently altered blood; and that the "neurilemma was inflamed." Since then several observers have examined the ganglia at different periods after an eruption of zoster. Charcot and Cotard (1865) found injection and inflammatory exudation into the ganglion, but the case is insufficiently reported. Oscar Wyss (1871) and Sattler (1875) in *H. ophthalmicus* found haemorrhage and infiltration into the Gasserian ganglion. Lesser (1881) in three admirably reported cases of ordinary zoster found haemorrhages into a ganglion. Dubler examined a case of zoster secondary to necrosis of the ribs, and found changes in three intercostal nerves. He also, in an ordinary case, found haemorrhages in one ganglion.

Dr. Campbell and I took up the question, not so much to determine the nature of the lesion in zoster as to define the central representation of the affected areas of the skin. We obtained 21 necropsies at all periods, from a few days to a year and a half, after the eruption. In the acutest cases we found haemorrhages into the ganglion destroying it in part. These haemorrhages were not usually of large size, but were surrounded by a considerable amount of inflammatory exudation. The ganglion-cells were destroyed to a varying extent, and in the later cases parts of the ganglion were much sclerosed.

Secondary to this destruction of the ganglion-cells there was more or less definite degeneration of the peripheral afferent nerves, and considerable change in that posterior spinal root in connexion with the affected ganglion. This was beautifully shewn by the Marchi method, and could be followed for some distance upwards in the posterior column of the spinal cord. Zoster thus enabled us to determine definitely the supply of the posterior-root ganglia; for in the acute stage the area affected on the skin was mapped out, and after death we determined the posterior root to which this area belonged by the degeneration that it shewed when stained by Marchi's osmic acid method. In this way Dr. Campbell and I have traced the following root-areas (*vide* Figs. 71 and 72):—cervical 3 (twice), cervical 4, dorsal 2, dorsal 4 (twice), dorsal 6 (twice), dorsal 7 (twice), dorsal 8, dorsal 11, dorsal 12 (three times), and lumbar 1. Now if these areas are correctly named on Figs. 71 and 72, as seems to be the case, it is probable that the remainder of the areas on the figure are correctly shewn, although they have not yet been verified on necropsy. We also examined three cases of zoster within the territory of the trigeminal, in all of which we found changes in the Gasserian ganglion.

Thus it seems certain that herpes zoster is associated with an acute inflammation of, or haemorrhage into, the posterior-root ganglion, followed by more or less secondary degeneration in the posterior root and peripheral nerves connected with that ganglion.

**Symptoms.**—Some malaise generally precedes the first appearance of the rash, particularly in children. The child is ill; it lies about by day

and tosses restlessly at night. It vomits, or refuses food, and the mother suspects the onset of some acute specific disease. Adults may suffer from a slight rigor with shivering and chilliness, similar to the rigor that accompanies the onset of acute lobar pneumonia, but of less intensity. During this period the temperature generally rises somewhat; as a rule in adults it does not exceed  $100.5^{\circ}$  F., but in children it may occasionally reach  $102^{\circ}$  F.

Pain is usually present from the first; it is shooting in character and worse at night. Thus, it is not uncommon for these cases presenting some fever, malaise, and pain in the side to be admitted to hospital for acute pneumonia or pleurisy; and the true nature of the disease may not be evident until the rash appears about the fifth day. The pain follows the lines of the nerve-roots, and occupies the territory not only of the anterior primary division (intercostal nerves), but also of the posterior primary division. On the trunk it thus runs more or less straight round one-half of the body. The pain may be associated with some hyperalgesia; and on more than one occasion I have been fortunate enough, by means of the antecedent hyperalgesia, to mark out the area of the coming herpetic eruption.

With the appearance of the rash the temperature may fall and the general malaise decrease, although the pain remains. But this is by no means always the case; for it would seem that the period in the disease at which the rash appears is extremely variable, and the best method of considering the course of a case of zoster is to date the beginning of the attack from the first onset of pain and malaise. Almost every patient suffers from considerable pain, and the majority from some fever and general discomfort.

The rise of temperature lasts from three to five days, and this may be considered as the duration of the acute disease. The rash may appear a few hours after the onset of the disease, or may be delayed until the period of the acute general symptoms is past. Thus, if the rash be taken to represent the physical signs, an attack of zoster bears a close resemblance to an attack of acute lobar pneumonia; for it is notorious that the signs in the lungs may be present very shortly after the initial rigor, or may not make their appearance until the crisis has been reached.

The rash most commonly appears on the third or fourth day of the disease, just as the physical signs of acute lobar pneumonia usually present themselves on the third or fourth day after the initial rigor. From the time when it first makes its appearance the rash spreads with very varying rapidity. In each area representing the distribution of a posterior root three spots usually exist at which the branches come to the surface (posterior primary, lateral branch of anterior primary, and anterior branch of anterior primary division). It is over these "maxima" that the eruption first makes its appearance. From these points it spreads along the whole area of the distribution of the main branches, and may invade the distribution of even the finest twigs,

until, in a complete case, the whole area of one posterior root is occupied by vesicles or a raised erythema. The most severe incidence of the eruption always falls on the skin in the neighbourhood of the maxilla; and it is over these points that in the severest cases huge bullae (sometimes containing blood-stained fluid) or small gangrenous patches may appear. Sometimes the territory of the anterior primary division, sometimes that of the posterior primary division, is first affected: no definite rule can be laid down. The large majority of cases do not run a severe course; and in some the whole eruption consists only of a few vesicles scattered around one or more of the maximum spots.

On the palm and sole of the foot vesicles are extremely rare. When present on the palm and sole they tend to be of small size, very little raised, and not surrounded by erythema. Vesicles on the fingers, the back of the hand, the toes, and the dorsum of the foot are not often, in my experience, severe.

The rash may come out fully in two days from the appearance of the first spot, or may continue to come out for a week. The latter is particularly apt to be the case if the outbreak of the rash occur synchronously with the onset of the fever and malaise. On the other hand, in those cases in which the rash is delayed until the fall of temperature, the whole eruption may come out with extreme rapidity.

The rash may consist, from the first, of vesicles containing clear fluid, surrounded by more or less erythema; but more commonly it first shews itself as an erythema upon which vesicles rapidly arise. The whole of the distribution of the posterior nerve-root is rarely, if ever, occupied by vesicles; and the whole distribution can only be obtained by including the borders of the profound erythema. In very severe cases the vesicles may contain blood-stained black fluid. Sometimes these rapidly break down and give place to shallow ulcers, that may reach the size of a florin. In all such cases the subsequent scarring is profound, and much after-pain is likely to result. In most cases the contents of the clear vesicles become turbid. Possibly it is in connexion with this pus-formation that the lymphatic glands that drain the affected tract of skin are in the majority of cases enlarged. *H. zoster* thus forms a useful means of determining the distribution of the lymph-channels from skin-areas. During this time the temperature may remain a little raised ( $99.2^{\circ}$ - $100^{\circ}$  F.), possibly owing to the invasion of the vesicles by the organisms of suppuration.

About the fifth to the tenth day after their first appearance the vesicles begin to dry up and to form scabs. Under these scabs the eruption heals, and at the end of six weeks beyond some <sup>as</sup>freshly healed scars nothing is to be seen. Some leave scarcely any scarring, although the scars of the severer eruptions are large, irregular, and white—closely resembling those made by a superficial burn.

The pain which precedes the rash has already been described. During the period of the rash itself the pain becomes more local in distribution, and may be little more than a painful itching; or it may



become of an agonising burning character. When severe it is worse at night, and in such cases the patient suffers from loss of sleep.

Usually the pain dies away when the rash begins to heal; but in elderly patients it may last for weeks, or even for months and years, after the scars are healed. In such circumstances the pain is stabbing, darting, and aching, and is seated in the position of the heaviest scarring. I have not seen this pain follow herpes, except in elderly people or where there was considerable scarring. It is relatively more common after herpes of the ophthalmic division of the trigeminal, and in this situation severe cases may occur in young adults, especially if the rash have left deep scarring. The pain, although subject to exacerbations, is usually continuous; and I have not as yet seen a case in which the pain assumed the paroxysmal character common in neuralgia quinti major ("Tie douloureux," p. 543). It tends to vary from day to day, and, like the lightning pains of tabes, is worse "when the weather changes." The exact nature of the meteorological change that increases these nerve-root pains is not yet determined.

After the rash has died away the skin it has occupied not infrequently remains abnormally tender to painful stimuli, such as the point of a pin dragged lightly across it. But where there is a deep and widespread scarring all forms of sensation, but particularly sensibility to heat and cold, may be diminished. This loss of sensation does not extend over the whole area previously occupied by the rash, but seems to be limited to the part where the scarring is deepest. Thus, it cannot be due to a complete degeneration of the nerve-fibre, but only to a loss of those fibres which supply the parts most deeply affected. Apart from coincident nervous disease, I have never seen a broad band of anaesthesia extending over the whole area previously occupied by the rash as a consequence of an attack of zoster.

Second attacks are very rare, apart from nervous disease. I have personally met with 4 cases in which a patient with zoster has shewn scars of a previous attack. One of these cases is well authenticated, as it occurred in the person of an eminent dermatologist. In none of these cases did the distribution of the second attack coincide with that of the first. Similarly it is rare for a patient to be the subject of a bilateral eruption, apart from the coexistence of some gross disease of the central nervous system. Kaposi mentions a bilateral case; and I have also seen one in which the eighth dorsal was affected on the left side, the tenth dorsal on the right. In no case of spontaneous zoster has the bilateral eruption been at exactly the same level.

**Zoster of the Head and Neck.**—Within the territory of the first or ophthalmic division of the fifth nerve herpes, exactly resembling in course that seen on the body, is a fairly common occurrence. It is preceded by considerable malaise and some rise of temperature, and is noteworthy for the extreme severity of the pain. The area occupied by the rash is either a part or the whole of the distribution of the ophthalmic division. It may extend as far back as the parietal eminence, and occupy



the whole upper lid and side of the nose as far as the ala nasi. This implication of the side of the nose is an extremely important feature; for, as Sir J. Hutchinson first pointed out, the patients in whom this area of the skin is affected are peculiarly liable to suffer from ulceration of the cornea. The rule as originally laid down by Sir J. Hutchinson is too absolute; for Hybord found that out of 53 cases in which the nose was affected 35 shewed eye changes, whilst in 18 the cornea and iris were normal. Fig. 69 shews the invasion of the nose; in Fig. 70 the whole ophthalmic division is affected, excepting the branch to the side of the nose.

When the eye is affected the conjunctiva becomes red and injected, and ulcers may appear on the cornea; it is probable that the abrasions occasionally seen on the inflamed conjunctiva are the remains of similar shallow ulcers. But the cornea is not the only structure of the eye that is apt to suffer in herpes of the ophthalmic division of the fifth. Iritis also is apt to occur, and, unless care is exercised and the pupil kept under the influence of atropine, adhesions may form between the posterior surface of the iris and the anterior surface of the lens. Panophthalmitis has also been described in several cases.

Although I have carefully examined every case of H. z. ophthalmicus that has come under my notice, I have never seen changes in the retina or optic nerve, even in the most severe cases of this disease. Blindness has, however, been known to follow an attack (Bowman).

In rare instances paralysis of the ocular muscles and ptosis have accompanied the disease. In some of these cases the herpes was not of the true spontaneous type, but was secondary to some growth or disease about the base of the skull (Sattler). But there are several cases on record (*vide* p. 490) in which ophthalmoplegia interna and externa accompanied the spontaneous zoster of this distribution. In one case that came under my notice (Silcock) a careful naked-eye necropsy failed to reveal any gross disease of the eyeball, nerves, or base of the brain. Removal of tissue for microscopic examination was unfortunately not permitted.

Ramsay Hunt has shewn that inflammation of the geniculate ganglion may be the cause of a true herpes. In this case the eruption is situated over the auricle and within the meatus. This form is frequently associated with paralysis of the facial nerve.

Herpetic eruptions about the lips and nose, or on the cheeks, are common in connexion with febrile states, or with inflammation of the nose and pharynx. Such eruptions, however, bear no relation to zoster; for (*a*) they are usually bilateral, (*b*) they notoriously tend to recur frequently. Thus, some patients are subject to this disease whenever they are attacked with a common nose cold. (*c*) Herpes labialis may occur concomitantly with zoster on the trunk. Now double zoster is one of the greatest of rarities; whereas on several occasions I have seen typical H. labialis present in a patient suffering from a well-marked attack of zoster on the trunk. (*d*) H. febrilis is not accompanied or preceded by the characteristic neuralgic pain of H. zoster.

Yet, in spite of this, true zoster of the face characterised by unilaterality and subsequent scarring does exist. In one such case Dr. Campbell and I found a haemorrhagic focus in the Gasserian ganglion exactly analogous to the changes in the posterior-root ganglion which we found in the other cases of zoster which we examined after death. Moreover, in one case I saw typical *H. ophthalmicus* associated with an equally well-marked eruption over the area of the second division (infraorbital) of the trigeminal.

I have also seen several cases of true zoster involving the third or



FIG. 69.



FIG. 70.

maxillary division of the fifth nerve. However, true zoster over the area of the two lower branches of the fifth is rarer than *H. ophthalmicus*.

Thus it will be noticed that zoster on the face tends to follow the distribution of the three main peripheral branches of the ganglion rather than to be distributed over the supply of "root areas" or "segments." This is probably due to the structure of the Gasserian ganglion; for this ganglion is the homologue of a large number of posterior-root ganglia. Though an anatomical integer it is physiologically manifold. Thus to anatomical lesions it reacts on coarse anatomical lines; to physiological stimuli it reacts over much smaller areas corresponding to the ancient supply of its components.

**Herpes of the Tongue.**—The tongue is occasionally the seat of a true herpes, but the vesicles are extremely rapidly broken, giving

## EXPLANATION OF FIGS. 71, 72.

Figs. 71, 72 shew the distribution of the segmental areas from the 3rd cervical to the 4th sacral zone. The form and dimensions of each area (which is drawn here) are derived from :—

1. The relative appearance of the tender skin in visceral disease.
2. The distribution of the eruptions in 412 cases of herpes zoster.
3. The limits of the analgesia (or loss of pain) in organic diseases of the spinal cord and spinal roots.

C 3=Sterno-mastoid or 3rd cervical area.

C 4=Sterno-nuchal or 4th cervical area.

Here follows a blank which is not generally represented in visceral diseases. The same corresponds with 5th, 6th, 7th, and 8th cervical segment.

D 1=Dorso-ulnar or 1st dorsal area.

D 2=Dorso-brachial or 2nd dorsal area.

D 3=Scapulo-brachial or 3rd dorsal area.

D 4=Dorso-axillary or 4th dorsal area.

D 5=Scapulo-axillary or 5th dorsal area.

D 6=Subscapulo-inframammary or 6th dorsal area.

D 7=Subscapulo-ensiform or 7th dorsal area.

D 8=Middle epigastric or 8th dorsal area.

D 9=Supra-umbilical or 9th dorsal area.

D 10=Sub-umbilical or 10th dorsal area.

D 11=Sacro-iliac or 11th dorsal area.

D 12=Sacro-inguinal or 12th dorsal area.

L 1=Sacro-femoral or 1st lumbar area.

L 2=Gluteo-crural or 2nd lumbar area.

Then follows a second blank, which is not primarily represented in visceral diseases. It corresponds to the 3rd and 4th lumbar segment area.

L 5=Fibulo-dorsal or 5th lumbar area.

S 1=Sole or 1st sacral area.

S 2=Sciatic or 2nd sacral area.

S 3=Gluteo-pudendal or 3rd sacral area.

S 4=Coccygeal or 4th sacral area.

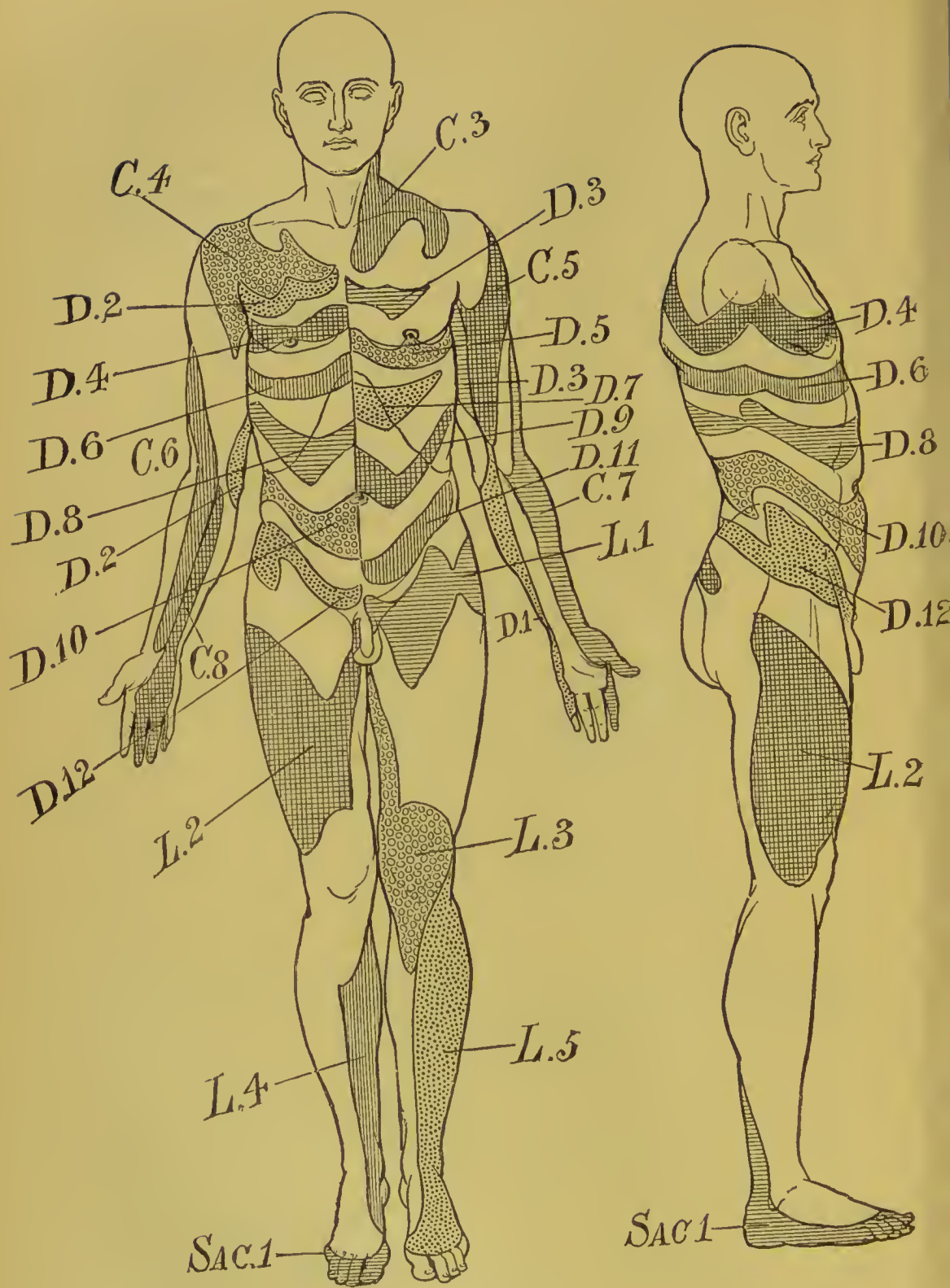


FIG. 71



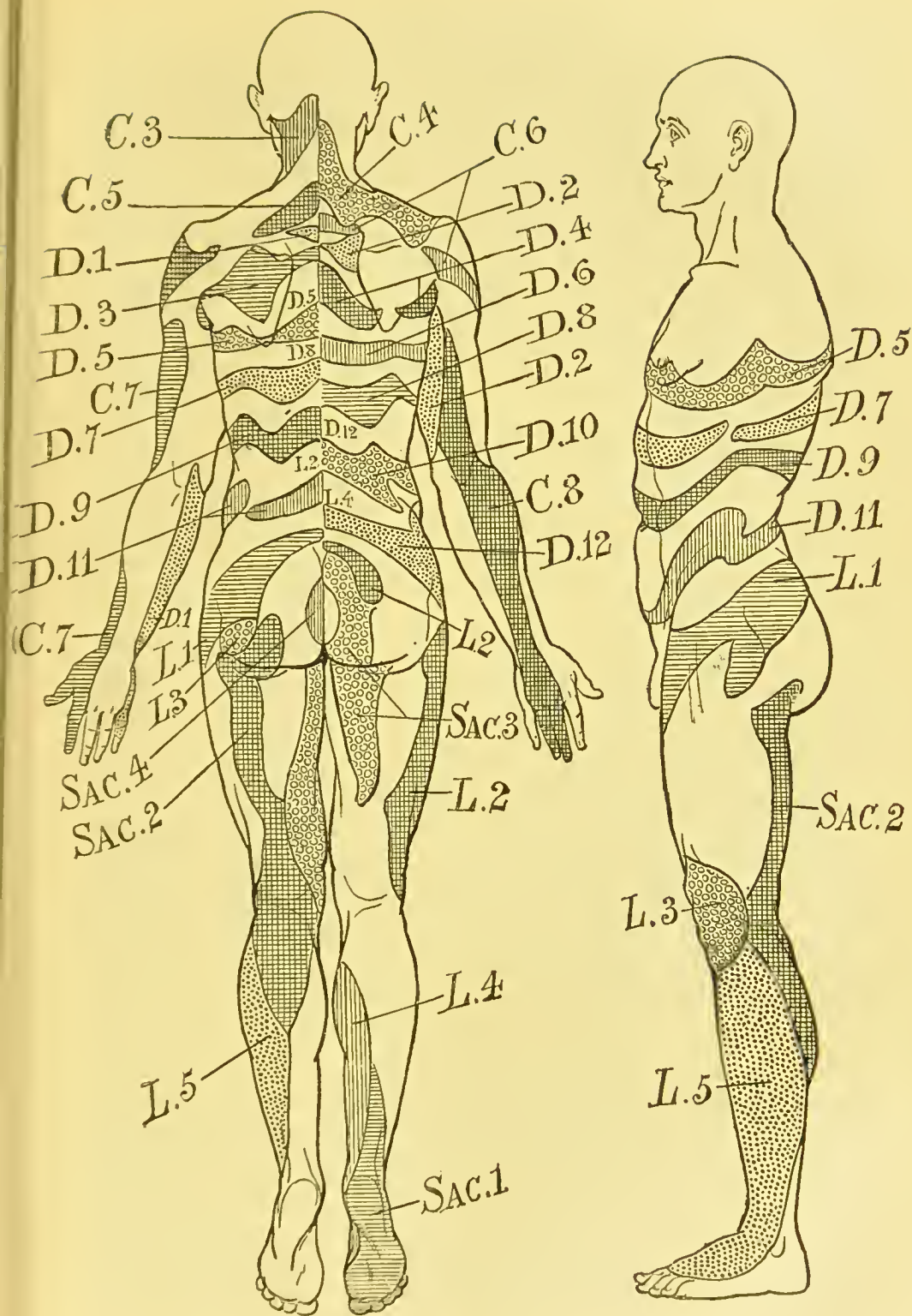


FIG. 72.

place to shallow ulcers. Occasionally the original vesicular nature of the affection can be seen in the ragged remains of the vesicle still adhering to the edge of the ulcer. The ulcers are usually distributed on the upper surface of the tip of the tongue, but occasionally they occupy a strip along the dorsum, not reaching either the side or tip.

The tongue is apt to be affected in connexion with the lips, and in such cases the eruption is frequently bilateral. It thus breaks two of the canons of true zoster, and is undoubtedly, in most cases, of the same nature as *H. labialis*. I have, however, though rarely, seen cases in which the eruption was unilateral, and was not associated with an eruption on the lips or palate. Such cases may be of the nature of true zoster; but the usual cases on the tongue are certainly manifestations of *H. febrilis* (or *labialis*).

The hard palate may also be the seat of herpetic eruptions, but these are usually bilateral and tend to recur.

**Herpes of the Neck.**—I pointed out above that the lateral and posterior regions of the neck, in fact all that part of the neck situated posterior to a line carried roughly along the anterior border of the sterno-mastoid, could be the seat of zoster as typical as any on the trunk. It is unilateral, occurs once only, and is accompanied by the typical neuralgic pain and more or less malaise.

The area in front of the sterno-mastoid can also be the seat of true zoster, but is rarely attacked without the simultaneous invasion of the third cervical area. When attacked by true zoster the region of the great occipital nerve is usually also affected (second cervical).

On the other hand, herpetic eruptions of the type of *H. labialis* are not infrequent within this area. They are not infrequently associated with spots and vesicles about the lips, and are commonly bilateral.

**Distribution of Zoster.**—Mehlis, in 1818, was the first to suggest that the eruption of *H. zoster* follows the distribution of nerves, but von Bärensprung was the first to prove this hypothesis. He stated definitely that the eruption of *H. zoster* followed the distribution of the fibres from a posterior-root ganglion. But throughout his paper he names the various eruptions according to the peripheral nerves they affected, as the distribution of the fibres of the posterior root was then unknown. Thus the erroneous doctrine grew up that herpetic eruptions follow the distribution of peripheral nerves. As each case arose the teacher pointed out how it followed this or that nerve in a more or less satisfactory manner. It was, however, obvious to any one who examined such cases carefully, especially when the disease happened to attack one of the limbs, that it certainly does not follow the course of any peripheral nerve. Dr. James Mackenzie and I simultaneously saw the importance of a more careful study of the distribution of these eruptions. For, if v. Bärensprung's statement were correct, the distribution of these eruptions would be an admirable method of studying the supply of certain fibres from the posterior roots. That v. Bärensprung was right in his statement of the pathology of the disease has

been amply borne out by necropsy (*vide* p. 476); and in describing the areas affected by *H. zoster*, I shall assume its correctness.

In a very large proportion of the cases the eruption does not occupy the whole area of a single nerve-root, but a district consisting of the maxima, surrounded by lines or patches of vesicles of variable extent. Thus it is only by collecting a large number of cases that it is possible, even approximately, to determine the extent of any one root-area.

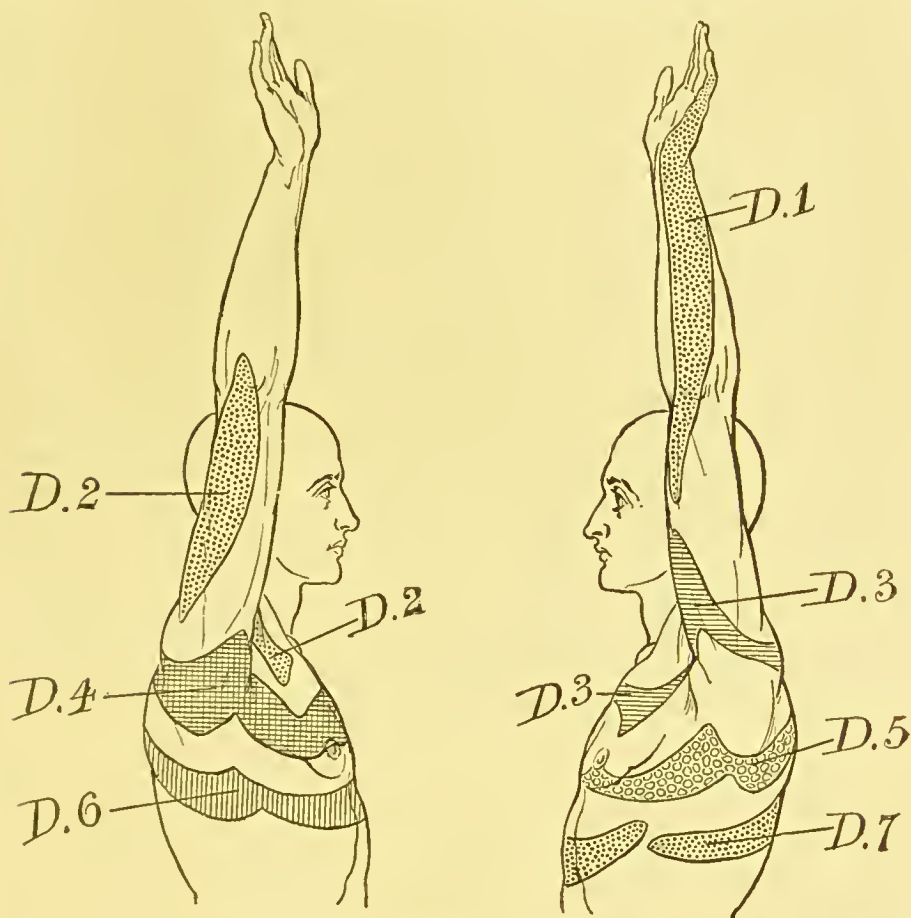


FIG. 73.

Figs. 71, 72, 73, and 74 shew the distribution of the fibres from the posterior-root ganglion based upon the 412 cases of zoster of which I have photographs or drawings. There is no pretence to absolute accuracy, for such accuracy could only be obtained by reproducing the distribution of each area separately. But the area affected in each case is a band coiled round one-half of a rough cylinder, and it is obvious that the shape assumed by this band will vary greatly with the diameter of the cylinder. Thus, a nerve-root area spread out on the round belly of a baby will have quite a different appearance from the same eruption

around the waist of a woman. The same eruption will differ considerably as it is extended on the long, narrow, sloping chest of the phthisical, or the barrel-shaped, high-shouldered trunk of the emphysematous patient. Bony points are thus almost useless as landmarks. Skin points only are trustworthy, and of such landmarks on the trunk we unfortunately possess only the nipples and the navel.

We are also confronted with a second difficulty which must make combined figures such as 71 and 72 untrustworthy; namely, that the supply from any one root may vary. Thus, in two several patients a certain portion of the skin may be supplied by a higher or by a lower root. The nervous system may be "prefixed" or "postfixed." Such variation is best seen by studying those areas which just lap on to the limb,—the third dorsal on the arm and the first lumbar on the leg. Now an examination of 34 cases of zoster over the third dorsal, and of 27 cases of zoster over the first lumbar, has led me to the following conclusions:—The third dorsal usually extends about  $\frac{3}{4}$  of the distance down the inner aspect of the arm, ending in the adult at a point about 3 in. above the elbow. But in some cases it may extend as far as the inner condyle of the humerus, and if so the posterior portions of this area tend to lie high, and to leave a considerable portion of the lower part of the scapula uncovered (prefixed). In the other extreme variation the third dorsal only just laps on to the arm close to the insertion of the pectoralis major; in such cases the posterior patch closely resembles that usually formed by the 4th dorsal, and covers the scapula down to the angle (postfixed). A third difficulty arises from the comparative rarity of zoster over certain root-areas. Thus, I have seen too few instances of eruptions over the 6th, 7th, 8th cervical, 3rd, 4th, and 5th lumbar, and 1st sacral, to do more than guess at the real supply of these roots.

The following table shews the relative frequency in my experience of 416 cases with which each area is affected:—

Trigeminal—			Dorsal VI.			20
1st Division	18		" VII.			19
2nd "	2		" VIII.			36
3rd "	2		" IX.			19
Cervical II.	1		" X.			26
" III.	15		" XI.			22
" IV.	21		" XII.			18
" V.	2		Lumbar I.			27
" VI.	3		" II.			22
" VII.	5		" III.			5
" VIII.	0		" IV.			1
Dorsal I.	5		" V.			2
" II.	9		Sacral I. [in combination].			
" III.	34		" II.			1
" IV.	38		" III.			5
" V.	38					

This table shews also the frequency with which areas of the trunk



are affected compared with the roots that supply the terminal portions of the limbs.

Occasionally more than one ganglion is affected, and two root-areas are then affected by the eruption. This occurs most commonly with the three upper cervical ganglia, and cerv. 2, cerv. 3, or cerv. 3 and 4 may be affected together.

Severe eruptions of zoster may overlap the middle line in front and

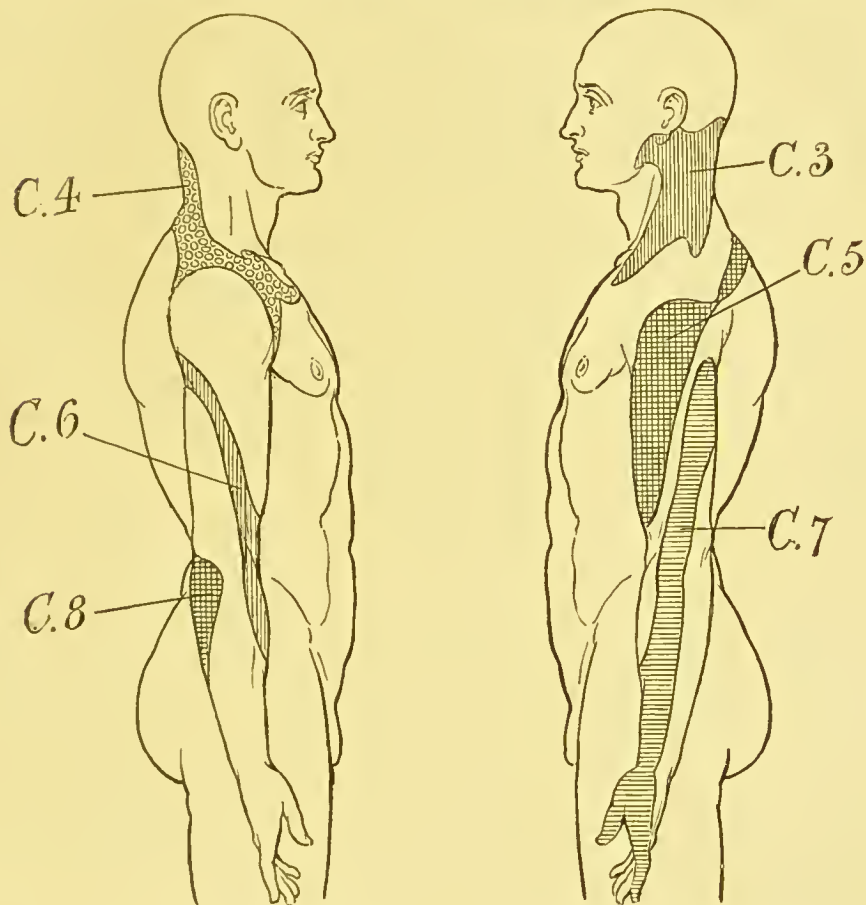


FIG. 74.

Figs. 71, 72, 73, 74 represent diagrammatically the areas over which zoster makes its appearance. The nomenclature of each area refers to the posterior-root ganglion affected in each case. Thus C. 3 represents the supply of the 3rd cervical, D. 3 that of the 3rd dorsal, L. 3 that of the 3rd lumbar, and S. 3 that of the 3rd sacral.

behind for from about 1 to  $1\frac{1}{2}$  inch. As a rule, however, this overlapping portion consists of erythema only, and is not covered by vesicles.

The upper and lower borders of an eruption cannot be accurately represented by hard lines, as on Figs. 71, 72, 73, and 74. The edges are serrated with many larger and smaller notches, produced by the incidence of the eruption over terminal nerve-twigs, which tend to run not only

horizontally, but also downwards to an extent varying with every area.

Thus, the overlapping of any two areas above and below is less than has been supposed, when this factor and the above-mentioned variations are taken into account. This is best seen in the relation of the 4th and 5th dorsal areas to the nipple: the 4th sends a limb downwards on the other side, and another on the inner side of the nipple, it supplies the upper portion of this structure; the 5th, on the other hand, always has an upper projection to supply the lower part of the nipple. Thus, when the breast is enlarged, as in women, the 4th dorsal covers roughly the outer, upper, and inner quadrants, whilst the 5th covers the lower quadrant. In the same way, however low the main portion of the 9th dorsal may lie, it always swings up to a point in the mid-ventral line above the level of the umbilicus; but the 10th dorsal never reaches the mid-venter above this line.

Overlapping is, however, greater on the limbs, and over such parts as the upper three intercostal spaces, and the pubes, where developmental compression has taken place.

**Complications of Zoster.**—*Skin.*—The rash usually heals up and leaves scars within a few weeks; but occasionally gangrenous sores may appear, and may last for many weeks, or even months. In a lunatic patient I once saw these sores last for over a year; but this probably was due to the irritation of his filthy habits.

The outbreak of zoster seems to be quite uninfluenced by the simultaneous existence of other skin conditions. Thus, I have seen an attack of acute zoster in a patient who was covered with an extensive and well-marked macular syphilide. The zoster was unaltered in distribution or appearance, and died away in the usual time and manner. Zoster of the typical appearance is not uncommon in patients suffering from psoriasis, possibly owing to the almost universal treatment of this disease with arsenic. One case that came under my notice was complicated by the coexistence of chicken-pox: the boy was obviously ill with vomiting, pain in his side, and a temperature of  $101^{\circ}$  F.; the day after his admission to the hospital (on the fourth day of his illness) an eruption of zoster appeared on the 5th dorsal area, and twenty-four hours afterwards typical chicken-pox spots came out over the arms, face, and chin, yet the herpetic rash was in no way altered by this complication.

**Motor Effects.**—Occasionally, though rarely, an attack of zoster is accompanied by motor paralysis (Ebstein). Thus, I have seen one case in which an eruption over the first dorsal area was accompanied by paralysis of all movements of the hand and fingers. This is particularly interesting when we bear in mind that the motor portion of the first dorsal root, together with that of the 8th cervical, innervates the intrinsic movements of the hand.

Herpes ophthalmicus also may be associated with paralysis of the movements of the eye (Hutchinson, Bowman, Blachez). I have seen two such cases (Silcock) in which complete ophthalmoplegia, externa

and interna, followed an eruption of this distribution. In one of them a naked-eye examination, after death, of the eyeball, optic nerves, and base of the brain failed to reveal any gross lesion.

Facial paralysis has been seen to accompany H. zoster, especially when it affects the occipital region and the area on the front of the neck (2nd cervical). Eichhorst has collected 18 such cases, and an extremely well-marked example has come under my observation. Zoster appeared over the 2nd and 3rd cervical areas after six days' prodromal pain and malaise. Two days afterwards the facial nerve on the same side became paralysed. The paralysis was of the Bell type, and was followed by loss of the faradic excitability of the muscles of the face and right half of the side of the forehead. Taste was unaffected. Ramsay Hunt has pointed out that herpes of the auricle and external auditory meatus is peculiarly liable to be associated with facial paralysis. This he attributes to inflammation of the geniculate ganglion.

*Affections of Deep Structures.*—It is a noteworthy phenomenon that, although a deep structure like the iris becomes inflamed in H. ophthalmicus, I have never been able to find any evidence of inflammation of the pleura or peritoneum in those cases in which the eruption lay around the chest, or over the abdomen. In the former group of cases I have habitually listened for signs of pleurisy, but have been unable to hear a friction sound; and in a necropsy on one such case I examined the parietal pleura carefully, but could not find any sign of inflammation. In a necropsy on a case in which the rash, present at death, occupied the 11th dorsal area, I was likewise unable to discern any inflammation of the peritoneum.

Again, there is no evidence that deep organs, receiving their visceral supply from the affected roots, become affected during an outburst of zoster. Thus, when the 10th dorsal is affected the testicle does not become tender in the same way that it does when in consequence of a renal calculus the 10th dorsal segmental area is hyperalgesic. With the exception of the iris, then, there is no evidence that any deep structure is affected during an attack of H. zoster.

*Treatment.*—In spite of many statements to the contrary, no treatment is effectual in aborting the eruption. Such statements are insusceptible of proof, for in a large number of cases the eruptions are incomplete.

When the rash has appeared it is well to dust it thickly with a powder consisting of starch 2 oz., oxide of zinc 1 oz., camphor powder 15 to 45 grains; and if there be much pain powdered opium (15 grains) is to be added. Another satisfactory application is ung. boracis (softened with the admixture of vaseline) 5 oz., cocaine 22 grains.

Ichthyol, either mixed with equal parts of water, or in the form of an ointment, is an extremely satisfactory preparation. In order to prevent rupture of the vesicles or the formation of sores they may be painted over with collodion.

For the after-pain, if severe, no treatment but morphine is adequate.

It is, however, always well to try antipyrin or pyramidon in 10-grain doses three times a day. General tonics, such as arsenic and quinine, are indicated, for the patients who suffer from the after-pain are always debilitated.

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H. H.

#### DISEASES OF THE SYMPATHETIC SYSTEM

By GORDON M. HOLMES, M.D., M.R.C.P.

It has been within only recent years that we have acquired any accurate knowledge of the anatomy and structure of the sympathetic system, thanks mainly to the work of Dr. Gaskell, Prof. Langley, and Dr. H. K. Anderson, and we are still very ignorant of the part the sympathetic nerves and ganglia take in the pathogenesis of disease. But as the sympathetic system innervates the unstriated muscles of the body, including those of the blood-vessels and intestines, the heart and the various glands, and in addition carries the afferent impulses from the viscera to the central nervous system, it seems very probable that its study in various constitutional and visceral diseases would be profitable.

Yet on looking through the history of medicine of the last century it may be seen that whilst in its earlier years many diseases were attributed to structural changes or functional disturbances of the sympathetic system, and even in the 'seventies monographs on the diseases of the sympathetic were written by Seeligmüller, Eulenburg and Guttman,



Meryon, and others, in recent years much less attention has been paid to it, and the older views that ascribed to the sympathetic nerves and ganglia considerable pathological importance have been largely discarded.

**Anatomy.**—It is chiefly to the work of Prof. J. N. Langley by physiological and anatomical methods that we owe a fairly full knowledge of the general structure of the sympathetic system. Its main part consists of a chain of ganglia lying in front of the spinal column, a pair connected with each pair of spinal roots from the first dorsal to the second or third lumbar in man, and with one another by a commissural strand. Each of these ganglia is connected with the corresponding spinal root by a white ramus, and each sends a grey ramus to the cerebro-spinal nerves; the prevertebral ganglia, which lie more distal on the sympathetic system, as the semilunar, do not supply any fibres to the somatic nerves. A second series of sympathetic fibres takes origin in the second, third, and fourth sacral segments. The cranial sympathetic system consists of visceromotor and viscerosensory fibres contained in the glosso-pharyngeal and vagus nerves, and in the nervus intermedius; and a few take origin in the third nerve nucleus for the supply of the intrinsic muscles of the eye through the ciliary ganglion.

All these parts Prof. Langley has included under the term *Autonomic System*. But the autonomic system is by no means independent, either structurally or functionally, of the central nervous system. The efferent sympathetic fibres probably take origin from the lateral horns of the spinal cord and pass out with the ventral roots, but they soon branch off from the somatic motor fibres in the white rami. These, the pre-ganglionic fibres, enter the vertebral ganglia and either terminate in them, give collaterals to them, or merely pass through them to end in one of the prevertebral ganglia. Each pre-ganglionic fibre terminates in a ganglion, and never passes directly to its peripheral organ. The cells of the ganglia, on the other hand, give origin to fibres that always pass directly to the organ they innervate. Efferent impulses from the spinal cord thus invariably undergo one relay, either in a vertebral ganglion or in a ganglion situated more distally in the sympathetic plexuses. The same statement holds for the cranial and sacral autonomic systems. There is apparently no differentiation of function in these ganglia; they are merely collections of cells for certain areas, and supply all kinds of fibres that pass from the system on which they are situated to that area. The afferent sympathetic fibres have their cells in the dorsal root or spinal ganglia, and the impulses pass from the peripheral end-organs to the spinal cord through a single set of neurons without undergoing any relay. The sympathetic ganglia have no afferent connexions and therefore cannot act as true reflex centres. Certain purely peripheral sympathetic reflexes, however, can be obtained; Prof. Langley has shewn that impulses may pass from the branches of one post-ganglionic fibre to those of another—axonal reflexes, or through the branches of the pre-ganglionic fibres—pre-ganglionic axonal reflexes.

The sympathetic ganglia also seem to have very little influence on

the tone of the smooth muscles they supply, as the loss of tone in the affected parts is usually no greater after section of the post-ganglionic fibres or removal of the ganglia, than after division of the corresponding pre-ganglionic fibres.

**THE CERVICAL SYMPATHETIC.**—The anatomy and physiology of the cervical sympathetic has been the most thoroughly studied, and disease of it produces more definite clinical symptoms than that of any other sympathetic nerve. Dr. H. K. Anderson and Prof. Herring have shewn that its fibres take origin from the cells of the intermedio-lateral tract from the eighth cervical to the fifth dorsal segment in the cat; in man it is probably less extensive. The fibres leave the cord by the corresponding ventral roots, but chiefly in the first to the third dorsal, and ascend the neck in the commissural strand to the superior cervical ganglion, which is the relay station for all the sympathetic fibres that supply the head (Langley). The post-ganglionic fibres leaving this ganglion join the upper four cervical, and the glosso-pharyngeal, vagal and hypoglossal nerves, but the majority join the sensory branches of the trigeminus. Other fibres pass into the cranium along the carotid artery to form the carotid and cavernous plexuses, from which fibres are distributed to the oculomotor and abducent nerves, and to the Gasserian ganglion. The pupillo-dilator fibres join the ophthalmic division of the trigeminus, and pass to the eye through the long ciliary nerves. Other fibres innervate the unstriated muscle of Müller which lies in the orbit and the upper lid.

Jonneseo, who stimulated the cervical sympathetic in man in 15 cases during the removal of the ganglia for the relief of epilepsy, obtained results which are in close agreement with those obtained from experiments on animals, namely dilatation of the pupil of the same side, slight exophthalmos, contraction of the vessels of the same side of the head and local sweating, but dilatation of the vessels of the mucous membrane of the mouth and palate, and increase of saliva and lacrymal secretion after a preliminary arrest. Stimulation also produced cerebral vaso-constriction. Section of the nerve, on the other hand, was followed by contraction of the pupil, retraction of the eye, narrowing of the palpebral fissure and pseudo-ptosis, congestion of the palpebral and bulbar conjunctivae, absence of sweating, but by a decreased surface temperature on the cheek of the same side. These are the chief clinical symptoms in man after section of the cervical sympathetic nerve.

**Etiology.**—The symptoms of *palsy* of the cervical sympathetic may be due to a lesion in any part of its course. Local lesions, such as tumours, myelitis, or traumatic injuries of the upper dorsal segments of the cord, may produce it, or compression or destruction of the corresponding ventral root fibres before the white rami branch off from them; this is not infrequently due to caries or a tumour of the vertebral column in this region. Oculo-pupillary symptoms are also occasionally associated with a lower brachial plexus palsy—the Klumpke type—which most commonly results from trauma, or from tumours growing in

this region. It is occasionally found with brachial plexus birth-palsies. Sometimes the fibres are damaged by a tuberculous process in the apex of the lung, or by an aortic aneurysm. In its course through the neck the sympathetic cord may be injured by wounds, or in surgical operations, or compressed by tumours or enlarged glands. Occasionally the pressure is due to the pressure of a goitre. Oppenheim observed hereditary cervical sympathetic palsy, and v. Michel has recorded a case of congenital affection.

*Symptoms.*—The oculo-pupillary symptoms are confined to the side of the lesion. The most constant is contraction of the pupil with maintenance of its reaction to light, though this is sometimes sluggish and small in range. Further, the contracted pupil does not dilate on shading the eye, or on stimulation of the skin of the cheek or neck, and it fails to enlarge when cocaine is instilled into the conjunctival sac. Still more prominent is a slight ptosis and narrowing of the palpebral fissure, due to paresis and loss of tone in the unstriated fibres which act as an involuntary elevator of the upper lid. On looking up, however, the ptosis disappears completely, and it has been consequently spoken of as pseudo-ptosis. A third symptom is slight enophthalmos or retraction of the eye; the exact explanation of this phenomenon, which is by no means constant, is doubtful. It has been attributed to atrophy of the orbital fat, but is more probably due to paresis of the unstriated fibres of the orbit, though these are poorly developed in man. A fall of the intra-ocular tension has been described, but it is rarely found in man, or even in animals under experimental conditions.

Vasomotor and secretory symptoms are rarely so prominent or so permanent as the oculo-pupillary, and as the fibres which subserve these functions take origin in the cord, mainly in the two segments below the origin of the oculo-pupillary fibres, these symptoms may appear dissociated. With complete paralysis there is usually dilatation of the vessels of the same side of the head and cheek, and particularly congestion of the conjunctiva. The temperature of the cheek is often definitely raised. Occasionally, however, the vessels of the cheek are contracted and its temperature is lower than on the sound side; in such cases the sympathetic lesion is mainly irritative. The flow of tears and saliva is sometimes increased for a time. Anidrosis of the corresponding side of the face is a very characteristic but inconstant feature; the skin becomes dry and scaly and does not sweat at all or to anything like the same extent as the normal side even after the administration of pilocarpine. As the cervical sympathetic supplies the sympathetic fibres to the first four cervical nerves, there is also absence of sweating on the same side of the neck and on the shoulder. Occasionally, however, there is an increase of sweating, but this is probably observed only in cases in which the lesion is partly irritative.

In some cases there is a slight wasting of the same side of the face, or rather a flattening out of the facial folds, especially of the naso-labial. Heiligenthal has attributed this to an atrophy of the subcutaneous fat,



but this does not appear a probable explanation. It has been observed that the hair becomes prematurely grey on the affected side, and facial hemiatrophy has been described following on a cervical sympathetic palsy. Section of the cervical sympathetic has apparently no influence on the heart.

Symptoms of *irritation* of the cervical sympathetic are less common; they are exactly the converse of those produced by its paralysis. The pupil is dilated, there is slight exophthalmos with retraction of the upper eyelid, and increase of sweating has been observed on the same side of the face.

*The Symptoms of Cervical Sympathetic Palsy associated with Lesions of the Medulla Oblongata.*—A short reference may be made here to a distinctive group of cases, in which contraction of the pupil, narrowing of the palpebral fissure, slight retraction of the eyeball, and often disturbance of the sweat secretion on the same side of the face, are associated with loss or diminution of pain and temperature sensibility on the opposite side of the body and often on the same side of the face, ataxia of the homolateral limbs and occasionally slight weakness of the opposite limbs, a tendency to fall towards the side of the lesion, nystagmus, vertigo, and some palsy of the muscles of deglutition, phonation, and articulation. These symptoms are almost always due to occlusion of one of the vertebral arteries or one of its branches, especially the posterior inferior cerebellar artery. The occurrence of the definite and characteristic symptoms of a cervical sympathetic palsy in these cases is explained by the existence of a superior sympathetic centre in the medulla, probably in the *formatio reticularis* near the floor of the fourth ventricle. The existence of this centre was originally demonstrated by Budge by experiments on animals. Its efferent fibres apparently descend to the spinal sympathetic centre; an interruption of these fibres explains the observation of Kocher, that lesions of the cervical segments of the spinal cord from which no sympathetic fibres take origin may produce the symptoms of a slight cervical sympathetic palsy.

After complete section of the cervical sympathetic, the paralytic symptoms generally continue indefinitely, but usually diminish in intensity; the recovery is usually greater in the blood-vessels than in the oculo-pupillary functions. There is no mode of treatment that can effectively influence recovery.

**THE VISCERAL SYMPATHETIC SYSTEM.**—Very little is known of the part the visceral sympathetic system plays in the production of disease, or even of the symptoms of severe lesions of the splanchnic nerves and the ganglia with which they are connected. In fact it has been found that section of the splanchnic nerves, and even excision of the solar plexus, do not produce any permanent affection of the functions of the abdominal visceral organs. Laignel-Lavastine (19) observed after removal of the solar plexus great hyperaemia of the abdominal organs, vomiting, diarrhoea, oliguria, slow pulse, and either death from collapse or slow



recovery. Popielski and others have kept dogs alive for several months after extirpation of the solar plexus, and noticed during their life only softness of the faeces and transitory glycosuria, but in animals killed within a short time of the operation there were, as a rule, haemorrhages and ulcers of the walls of the stomach, duodenum, and small intestine, with congestion and hyperaemia of all the abdominal organs. Strehl, who repeated these experiments in cats, obtained much the same results, but found that lesions in the mucous membrane are not necessary or constant. The only clinical symptoms were diarrhoea for a few days, in a few animals transitory albuminuria, and progressive weakness and loss of weight. He concluded that the only results of removal of the solar plexus are a too rapid emptying of the small gut and dilatation of the visceral vessels. In experimental peritonitis the pulse-rate was not influenced by section or removal of the solar plexus.

The afferent sympathetic fibres carry impulses which under normal conditions do not reach consciousness, but it must be remembered that in certain pathological states their impulses may affect consciousness; then the pain that results is referred not to the affected organ, but to certain regions of the surface of the body which receive their somatic sensory innervation from the segments of the cord into which the affected viscerò-sensory fibres enter. These are the *referred pains* which have been studied by Drs. Head, James Mackenzie, and others.

Certain clinical symptoms have been attributed to *neuroses or actual disease of the abdominal sympathetic*, especially by earlier writers as Romberg, Seeligmüller, and others, but the arguments in support of their views are not strong. Feiler has recently recorded two cases of what he regarded as sympathetic neuroses. Otherwise healthy patients had attacks of severe abdominal pain, generally referred to the region of the diaphragm, palpitation, and a feeling of suffocation accompanied by vague dread or the fear of death; in each case there was a spot exquisitely tender to pressure immediately below and to the left of the umbilicus, and pressure here induced these attacks. Triantaphyllidès has attributed similar symptoms to the same cause; he describes vertigo, vasomotor troubles, especially urticaria, paroxysmal abdominal pain, respiratory distress, vomiting and diarrhoea, and other intestinal disturbances, always associated with a *plaque ombilicale*, or a spot extremely tender to pressure at the umbilicus, to a neurosis of the solar plexus. These symptoms generally appeared in recurrent crises, but in some cases they were more or less constant. Müller ascribes to disease of the sympathetic loss of appetite, vomiting and diarrhoea, especially on emotional disturbance, anuria, jaundice, palpitation, and attacks of flushing and sweating. Engelhardt describes similar symptoms to which he believes the Jewish race are especially liable. Hoffmann assumes that disease of the solar plexus may produce pain in the epigastrium, which radiates into the sacral and gluteal regions, polyuria, and constipation. Certain forms of neurasthenia have also been interpreted as sympathetic neuroses; and Savill assumed that the sympathetic system plays a part in the

pathogenesis of hysteria. Certain vague abdominal pains, especially in neurasthenics, have been attributed to a sympathetic neuralgia, or a hyperaesthesia of the solar plexus.

But on the one hand there is no strong clinical evidence that it is to disease or functional disturbance of the sympathetic system that these symptoms are due, and on the other we are almost entirely without pathological evidence of sympathetic disease in these cases. There is, however, some evidence that certain abdominal symptoms may be due to sympathetic lesions. Laignel-Lavastine (20), for instance, discovered congestion, small round-celled infiltration and patches of necrosis in the abdominal ganglia, with chromatolytic changes or atrophy of many of their nerve-cells, in the majority of the cases dying from infective disease in which he examined these ganglia. These changes he is inclined to regard as the direct cause of some of the abdominal symptoms in infectious diseases. He also found sclerosis or inflammation of the solar plexus in different forms of mental disease, especially in cases with delusions of abdominal disease (21). In alcoholic and tuberculous polyneuritis the same changes were present in the sympathetic as in the cerebrospinal nervous system. D' Amato and Macri found parenchymatous and inflammatory changes in the sympathetic ganglia associated with acute and subacute gastritis experimentally produced in animals, and with chronic gastritis in man. In a case in which dyspnoea, ascites, and great enlargement of the liver were the most prominent symptoms, Stilling discovered neuritis of the splanchnic nerve, and regarded this as the causal factor.

The part played by disease of the sympathetic in the production of the symptoms of tabes is of great interest. Charcot originally attributed gastric crises to disease of the sympathetic, and Vulpian, Pierret, Fournier, and others adopted the same view. To Roux, however, we owe the most systematic investigation of the sympathetic system in this disease. He found extensive destruction of the myelinated afferent fibres, and to this he attributed the loss or disturbance of visceral sensibility characterising this disease. Heitz also found degeneration of many of the myelinated fibres of the cardiac plexuses, and correlated this with the cardiac analgesia, and the consequent well-known latency of cardiac and aortic disease in tabes. The investigations of Pal suggest that the symptoms of lead colic result from a vascular hypertension due to irritation of the abdominal sympathetic; Grasset (11) assumes a similar cause for the gastric crises of tabes dorsalis.

Only a short reference can be made here to the part the sympathetic plays in the pathogenesis of exophthalmic goitre and of Addison's disease. Many of the symptoms of the former are so similar to those that result from stimulation of the cervical sympathetic that efforts have naturally been made to invoke sympathetic lesions for its pathogenesis. Lesions of the cervical strand have been occasionally found, but further experience has not confirmed their importance. Dr. A. Bruce has, however, lately described congestion, capillary haemorrhages, and chromatolysis of the cells of the lateral horns of the upper dorsal segments in a case of acute

exophthalmic goitre. The part the sympathetic plays in the pathology of Addison's disease is less definitely determined; for whilst Bittorf, one of the most recent writers, concludes that alterations in the sympathetic have no significance, either in the production of the disease or of its individual symptoms, Wiesel has described degeneration of the chromaffin cells of the sympathetic ganglia, and believes that the disease is a specific affection of the chromaffin substance. Lichtwitz has observed somewhat similar changes in a case of Addison's disease with sclerodermia.

Various trophic and vasomotor neuroses have been also attributed to disease of the sympathetic system. In this connexion it is noteworthy that Dr. A. Bruce has found in two cases complete loss of sweating associated with lesions of the tractus intermedio-lateralis, the spinal origin of the pre-ganglionic sympathetic fibres; and Lannois and Porot have described extensive degeneration of these cells in a case of erythromelalgia.

Functional disturbances of the cervical sympathetic have been frequently assumed in *migraine*. Du Bois-Reymond observed on himself that on the same side as the unilateral headache the cheek was pale, the temporal artery contracted, and the pupil dilated. He therefore brought forward the hypothesis that his migraine was due to spasm of the muscular coats of the vessels supplied by the cervical sympathetic. Soon after, however, Möllendorff observed the converse signs in migraine, and postulated a temporary paresis of the cervical sympathetic. Definite pathological lesions of the cervical sympathetic have been, however, rarely found in migraine, and the work of recent years does not tend to support either hypothesis (*vide art.* Vol. VIII.).

It has been also assumed that the sympathetic, which probably regulates to some extent the cerebral circulation, may have an influence in the pathogenesis of epilepsy, and on this hypothesis the cervical sympathetic has been resected, or one of its ganglia extirpated, for the relief of this disease; the results have not justified the procedure.

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## DISEASES OF THE CRANIAL NERVES

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**Prefatory Note.**—In this article the cranial nerves are studied chiefly in connexion with their paralytic affections. Spasm, as it affects these nerves, is dealt with elsewhere, trigeminal neuralgia receives special consideration on p. 540, and labyrinthine vertigo is described elsewhere (Vol. IV. Part II. p. 525). Treatment will be dealt with on general principles only. For special forms of treatment the reader is referred to the articles upon diseases of the nose, throat, and ears.

**THE OLFACTORY APPARATUS.**—Situated in the Schneiderian mucous membrane is a large number of bipolar cells, whose protoplasmic processes ramify towards the surface, and whose axis-cylinder processes pass as olfactory nerves through the cribriform plate of the ethmoid bone. Entering the ventral surface of the olfactory bulb these fibres break up into end-tufts in the glomeruli of that body. In this situation they are in contact with the end-tufts of the protoplasmic processes of the so-called "mitral" cells of the olfactory bulb, whose axis-cylinder processes are continued along the olfactory tract towards the cerebral hemisphere. Some of the axis-cylinders of the "mitral" cells end in the cortex of the olfactory tract, the cells of which also send fibres to the hippocampal region and to the anterior commissure.

At the anterior perforated spot the olfactory tract divides into two roots, the external of which, passing towards the apex of the temporal lobe, contains fibres which end in the cortex of the hippocampal lobule; the mesial or smaller root is composed of the fibres which cross by the anterior commissure.



For a complete comprehension of the olfactory centres a study of this apparatus, as it occurs throughout the mammalian series, is essential. From such a study the following facts may be obtained :—

(a) All that remains in man of the rhinencephalon of macrosmatic mammals are the olfactory bulb and tract, the anterior perforated spot, the two olfactory roots, and the uncinate gyrus.

(b) In the anosmatics, such as the narwhal, the lobus hippocampi is a moderately well-formed structure. As this mammal does not possess an olfactory apparatus some other function must be fulfilled by it—a fact which indicates that this lobe is not concerned entirely with the sense of smell.

(c) The only structure which wholly disappears in the anosmatic mammal is, according to Dr. A. Hill, the *fascia dentata*, and this part varies with the relative development of the olfactory apparatus.

**Symptoms.**—*Anosmia*, or loss of the sense of smell, is a rare symptom of nervous disease. Much more commonly it is due to local conditions within the nose; hence the value of a careful rhinoscopic examination in all cases in which this sense is either blunted, lost, or perverted. In testing the sense of smell, substances should be used which stimulate only the olfactory nerve and do not irritate the trigeminal branches; such are oil of cloves, camphor, musk, and asafetida. *Anosmia* may be due to :—

(1) Local inflammatory and other changes within the nasal chambers.

(2) Arrest of secretion and “trophic” changes in the mucous membrane in cases of paralysis of the trigeminal nerve.

(3) Fracture of the base of the skull involving the ethmoid bone and the branches of the olfactory nerve which perforate it.

(4) Diseases involving the olfactory bulb and tract in the anterior fossa. Besides local meningitis, syphilitic necrosis, and bony tumours in this situation, unilateral anosmia is of value for the topical diagnosis of tumours of the frontal lobe (see also Vol. VIII. p. 40).

(5) *Hysteria* in association with hemianaesthesia and other stigmata characteristic of this disease.

*Parosmia*, or perverted sense of smell, and subjective sensations of smell are found along with local nasal disease. It has also been described in some cases of tumour involving the uncinate region of the temporo-sphenoidal lobe. It may form the warning of some epileptic seizures.

But for further consideration of this subject the reader is referred to the article on “Cerebral Localisation” in the next volume and to the article on “Nasal Neuroses” (Vol. IV. Part II. p. 60).

Concerning the treatment of anosmia little need be said. In the majority of cases it is the treatment of the local nasal condition: if, on the other hand, intracranial disease is present, treatment will be carried out on the appropriate lines.

**THE VISUAL SYSTEM.**—Course of the Fibres in the Nerve and Tract.—The optic nerves, chiasma, and tracts are composed of several bundles of fibres. The observations of Gudden, v. Monakow, Henschen,



and others have demonstrated the existence of a *direct bundle* of fibres passing between the eye and the central ganglia of the same side, and occupying the external part of the nerve. Upon the internal (mesial) aspect is found a second bundle, which is continued into the opposite optic tract, the *crossed bundle*; whilst, in a position relatively between the two, and occupying the more central parts of the nerve, is the *foveal* or *papillo-macular bundle*. The experiments of Usher and Dean, following upon similar researches by Pick, shew that secondary degeneration may be obtained in the optic nerve in the position of the macular bundle after experimental destruction of the retina between the macula lutea and the optic disc. At the chiasma the direct bundle occupies an external and also slightly superior situation, and maintains, in the more anterior parts of the optic tract, a relatively similar position, though Dr. Williamson's observation places it in a central position. The crossed bundle lies superior (Henschen) and inferior (v. Monakow) in the chiasma, internal and inferior in the optic tract; whilst the macular bundle, occupying the central part of each symmetrical half of the chiasma, lies in the middle of the optic tract. As these tracts approach the central ganglia the fibres of the several bundles intermingle, so that it has been found as yet impossible, by the degenerative or other processes, to distinguish the one from the other.

It is apparent from these observations that the fibres from the temporal halves of the retina (nasal field) occupy a corresponding (external) position in the optic nerve and tract; those from the nasal halves (temporal field) occupy a corresponding (internal) site in the optic nerve of the same and in the tract of the opposite side; the macular bundle occupying a relatively central position in both the nerve and the tract.

Having in this way ascertained the presence of these bundles let us now inquire how they arise and where they terminate.

According to the investigations of Ramón y Cajal and others upon young mammals, there exists in the retina a layer of large ganglion-cells, each of which has protoplasmic expansions, spreading in an horizontal direction in the internal plexiform stratum, and an axis-cylinder process which becomes an optic nerve-fibre. These axis-cylinders, passing by one or other of the bundles in the optic nerve and tract already described, reach the basal ganglia.

Optic tract fibres may be traced into three basal ganglionic structures: the anterior corpus quadrigeminum, the pulvinar thalami, and the external geniculate body. In the anterior quadrigeminal body the nerve-fibres do not appear to pass beyond the superficial stratum; but in the pulvinar and external geniculate body there is a more general disappearance of tract-fibres throughout the entire structure of these ganglia. In the external geniculate body the fibres of the crossed bundle of the nerve and tract form chiefly the ventral part of the capsular lining, whilst those of the direct bundle occupy the mesial and lateral aspects (Henschen). The anatomical description of these structures is corroborated by experimental and pathological results. Unilateral ocular ablation in

animals is followed by atrophy of the optic nerve and opposite optic tract, external geniculate body and pulvinar thalami, and of the superficial layer of the anterior quadrigeminal bodies. Enucleation of the eyeball in young animals is followed by atrophy of the cells in the superficial stratum of the anterior quadrigeminal body, while the cells of the pulvinar and external geniculate body remain intact. In an old-standing case of complete blindness, due to destruction of the eyeballs from small-pox in early life, Henschen observed atrophy of both optic nerves, the chiasma, and the tracts; atrophy of the cells of the external geniculate body and ventral part of the pulvinar thalami; atrophy of the optic radiations, chiefly the middle portion which is continued as part of the centrum ovale of the occipital lobes; and atrophy of the cortex of these lobes, more especially that of the calcarine fissure, and of Vicq d'Azyr's line.

It seems probable that the optico-pupillary fibres differ in size from the visual fibres, that they are of fine calibre, and that, although they occupy a definite position in the optic tract, they are in all likelihood distributed equally over the whole retinal surface, ending, according to Ramón y Cajal, in relation with the expansions of the bipolar cells of the internal granular layer; the visual fibres, on the other hand, of large size, take origin in the multipolar cells, and terminate in end-tufts in the pulvinar thalami and external geniculate body.

**The Optic Radiations and Posterior Visual Segment.**—A critical study of recent work upon this subject shews: (*a*) that lesions of the hind brain involving the optic radiations are followed by degeneration of these tracts, the external geniculate bodies, the pulvinar thalami, and the anterior quadrigeminal bodies; (*b*) that the fibres in relation with the calcarine fissure and the adjacent parts of the cuneus and lingual lobe occupy the middle and inferior portions of the optic radiations, and are distributed to the posterior and external parts of the pulvinar and external geniculate body—the most inferior of the strata in the radiations being localised in the lingual and fusiform gyri, the middle strata more especially in the cortex of the calcarine fissure; (*c*) that lesions involving the angular gyrus and convexity of the occipital lobe are followed by degeneration in the superior strata of the optic radiations, the anterior and superior parts of the optic thalamus and pulvinar thalami.

It appears, therefore, that the optic radiations of Gratiolet may be divided into three distinct strata, having definite relations with the basal ganglia on the one hand and the cerebral cortex on the other; and if the cortical centre of vision is limited to the lips of the calcarine fissure, the middle stratum of these radiations alone deserves this designation.

As a result of complete destruction of the external geniculate body, accompanied by slight secondary implication of the pulvinar and posterior part of the internal capsule, Henschen traced degeneration, on the one hand, through the middle and inferior parts of the optic radiations to the cortex of the occipital lobe; and, on the other hand, he found atrophy



of the optic tract on the side of the lesion and a degenerated strand in both optic nerves occupying the position of the direct and crossed bundles already described.

The visual path is therefore composed of two distinct segments, an anterior (inferior) and a posterior (superior). It is essential to bear this arrangement in mind when discussing the symptoms due to interference with the optic apparatus. The anterior segment consists of the optic nerve, chiasma, and tract. Of the fibres composing the optic nerve some come from the temporal side of the retina, others from the nasal side, and a third set from the papillo-macular region; at the optic chiasma some of the fibres pass directly into the optic tract of the corresponding side, while others decussate into the opposite optic tract; of the fibres which form the optic tract, some come from the superficial layers of the anterior quadrigeminal bodies, others pass into the external geniculate bodies, and a third set into the pulvinar thalami. The posterior segment is formed by the external geniculate body, pulvinar thalami, optic radiations, and cortical visual centres. Fibres pass out of the external geniculate body and pulvinar thalami as the optic radiations of Gratiolet; of which those occupying the superior layer of this radiation pass towards the cortex of the angular gyrus, those occupying the middle stratum towards the cortex of the calcarine fissure, and those of the inferior layer towards the cortex of the lingual and fusiform gyri.

**The Cortical Visual Centre.**—Henschen has located the cortical centre for vision in the cortex of the calcarine fissure. It is highly improbable, in view of many physiological and clinical phenomena, that the cortical centre is thus narrowly circumscribed. It would appear, indeed, from the observations already mentioned, that the cortical visual centre in man is situated in the cuneus, the calcarine fissure, and probably also the lingual and fusiform gyri.

The more extensive distribution of the cortical visual centre upon the surface of the brain has been recently confirmed. The researches of Dr. A. W. Campbell have localised the primary or "visuo-sensory" centre in the mesial aspect and tip of the occipital lobe; and a higher or "psycho-visual" centre has been located upon the external surface, the remainder of the cuneus and the lingual lobe.

**The Optico-pupillary Fibres.**—The course of the fibres subserving the pupillary light-reflex is not yet definitely known. There is sufficient evidence at hand, however, to shew that in the optic nerve lie two kinds of nerve-fibres, large and small; and it has been suggested that those of small calibre are more especially related to the action of the pupil. Beecher has stated that the pupillary fibres pass from the posterior border of the optic chiasma into the grey matter surrounding the third ventricle, and thence directly to the nucleus of the third nerve. But it is impossible to believe, in view of the hemiopic pupillary reaction which accompanies lesion of the optic tract, that all the pupillary fibres take this course. The histological investigations of Ramón y Cajal and Kölliker indicate that fibres leave the optic tract in front of or in the



neighbourhood of the external geniculate body, and terminate in the anterior corpus quadrigeminum. How the pupillary fibres reach the oculomotor nucleus is not known. Experimental ablation of the quadrigeminal bodies does not abolish the pupillary light-reflex in monkeys; and in some cases of lesion of these structures in man, the reflex action of the pupil has been retained.

**Symptoms of Disease of the Visual Apparatus.**—The several parts of the visual apparatus just described may be affected by disease. The causes and ophthalmoscopic appearances of optic neuritis and optic atrophy are described elsewhere (p. 340 *et seq.*).

*Optic Nerve.*—Besides optic neuritis and optic atrophy, as causes of failure of vision, the functions of the optic nerve may be destroyed by haemorrhage within the nerve sheath, trauma, and embolism of the central artery. As a result of such lesions vision may be impaired or lost.

In optic neuritis vision may remain unaffected, even with a considerable amount of swelling. On the other hand it may be lost suddenly. Hemianopsia may coexist with optic neuritis depending upon interference with the visual fibres in higher portions of the brain.

Loss of vision may be gradual, as occurs in primary optic atrophy from tabes and disseminated sclerosis. Such loss of vision does not necessarily take place throughout the whole extent of the visual field; on the one hand peripheral contraction may be found, or on the other hand loss of central vision only. In the former instances a perimetric chart shews a central area of clear vision around the point of fixation. Examples of the latter are seen in the cases of "toxic amblyopia," in which central vision, at first for colour and later for light in severe cases, may be abolished, but with good peripheral vision. The explanation of this would seem to be due to the implication of the papillo-macular bundle in the latter forms, as pathological examination of the nerve has shewn; in the former variety this bundle escapes, or is implicated in the late stages only.

In disease of the optic nerve the reaction of the pupil to light becomes impaired, and with the abolition of the light perception, the reflex pupillary contraction is arrested and the pupil dilates.

*Optic Chiasma.*—The arrangement of the fibres in this structure explains the symptoms brought out by disease. The characteristic symptom of lesion of the optic chiasma is *bitemporal hemianopsia*, due to interference with the fibres from the nasal halves of the retina.

The chiasma may be involved by tumours (syphilitic or other) in the pituitary fossa, and by dilatation of the third ventricle. Acromegaly, a condition accompanied by, if not actually due to, enlargement of the pituitary body, with secondary expansion of the pituitary fossa, is not uncommonly associated with bitemporal hemianopsia. Although lesion of the chiasma is accompanied by this form of hemianopsia, yet in practice various forms of scotoma are seen, due to unequal pressure upon, or unequal destruction of, its fibres. For example, blindness in one eye

may be associated with temporal hemianopsia in the other. In the later stages vision may be abolished in both eyes.

If a lesion involve the non-decussating fibres of the chiasma on one side, nasal hemianopsia results. A rare condition is *binasal hemianopsia*; cases of this kind have been recorded as a result of bilateral pressure from calcified carotid arteries.

It is well also to bear in mind that a growth in the pituitary fossa may reach a considerable size without causing any such localising symptoms as have been described.

**Homonymous hemianopsia**, or blindness of the corresponding halves of both retinae, may be due to interruption of the visual fibres in the optic tract, basal ganglia, and optic radiations, or to destruction of the centres in the cerebral cortex.

The line of demarcation between the seeing and the blind halves of the retina may or may not pass through the fixation point, which corresponds to the macular region, and is supplied by the papillo-macular bundle of fibres of the nerve. It is doubtful if the fixation point ever proves to be completely divided when carefully tested. If this be so, it is always included in the seeing, never in the blind half. There are various individual differences in the position and course of the dividing line. In some cases it is vertical, in others oblique; or it may be straight, or irregular. It is probable that these variations are due to peculiarities in the decussation of the optic fibres at the chiasma, rather than of lesions in particular localities.

It is not to be supposed, however, that there is a hard and fast line of demarcation between the portion of the retina supplied by the macular fibres and the general retinal area. In homonymous hemianopsia the blind halves pass over and involve a portion of the area supplied by the macular fibres.

In studying perimetrically a case of homonymous hemianopsia, in addition to the loss of vision in the correlated half-fields, more or less peripheral restriction of the seeing halves is not uncommonly found. This does not characterise lesion of any particular part of the visual path, for it may be met with from lesions situated anywhere between the optic chiasma and the cerebral cortex.

Although complete homonymous hemianopsia is the rule, several irregular and incomplete forms have been observed. Thus, a sector or *quadrant hemianopsia* has been described, in which corresponding retinal quadrants have been rendered blind. Drs. Beevor and Collier state that the line of separation between the visual centres corresponding to the upper and lower quadrants is probably the calcarine fissure, the lower visual field being represented in the upper or supra-calcarine area, and vice versa.

There are also various forms of *irregular hemianopsia*, giving peculiar perimetric tracings, which cannot be put down to any definite lesion, but which are probably due to local inflammatory or other destructive change in the retina, optic nerve, or tract. A *monocular hemianopsia*, due to partial

lesion of the optic nerve from fracture through the optic foramen, has been described.

In the vast majority of cases hemianopsia is absolute ; that is to say, there is loss of colour-, form-, and light-senses. In a case recorded by Vialat, complete hemiachromatopsia was associated with partial hemianopsia,—a condition, however, which passed into absolute hemianopsia before death. The loss of colour-sense may therefore be regarded as the earliest manifestation of implication of the visual centres ; and, depending upon the extent and intensity of the destruction, more or less defect of form- and light-senses is associated with it. In central colour-scotoma from toxic causes, loss of the senses of red and green may be looked upon merely as antecedents to complete loss of form and light, which latter are met with in severe and advanced cases.

**Diagnosis of Lesions of the Visual Path.**—Homonymous hemianopsia, occurring without any other associated localising symptom, is due to destructive lesion of the half-vision centre in the cerebral cortex, or of the subjacent optic radiations in the occipital lobe. Right-sided hemianopsia may or may not be associated with word-blindness or word-deafness. If such symptoms coexist the combination shews not only an implication of the optic radiations, but also of the cortical grey matter of the angular gyrus, the first temporal convolution, or both.

When hemianopsia is associated with hemianaesthesia and hemiplegia, the lesion is in the retro-lenticular part and in the posterior limb of the internal capsule. Destructive lesions of the basal ganglia are usually accompanied by hemianopsia. Henschen believes that destruction of the external geniculate body alone is productive of hemianopsia ; but the case from which he deduces this statement is by no means conclusive, as the pulvinar thalami was partially involved. Lesion of the optic tract causing hemianopsia may or may not be associated with localising symptoms, such as hemiplegia or paralysis of the oculomotor or other cranial nerves. There is one sign, however, which is supposed to be diagnostic of a lesion of the optic tract, and that is the hemiopic pupillary reaction.

**The Hemiopic Pupillary Reaction.**—This symptom, originally described by Wernicke, has been regarded as diagnostic of lesion of the optic tract.

When a narrow pencil of light is thrown upon the blind halves of the retinae no pupillary contraction is observed, or merely a sluggish one ; when, on the other hand, the light is turned on to the seeing halves the pupil contracts normally. This symptom, therefore, presupposes the existence in the optic tract of pupillary fibres corresponding to the visual fibres from corresponding retinal halves. The following conclusions have been drawn from the records of cases in which during life the hemiopic pupillary reaction was present :—

(a) That lesions involving the optic radiations do not give rise to the hemiopic pupillary reaction, unless indirectly by interference with the optic tracts.

(b) That lesions of the optic tracts, whether these parts are involved



directly or by pressure from a distance, are accompanied by this form of pupillary reaction.

(c) That lesions of the basal ganglia—external geniculate body and pulvinar thalami—do not of necessity give rise to the hemiopic pupillary reaction. They are not uncommonly associated with it, but merely by secondary implication of the tract fibres.

**THE OCULOMOTOR NERVES.**—Under this head are included the third, fourth, and sixth pairs of cranial nerves. These nerves may be affected by disease together or individually; and the symptoms thus produced may be unilateral or bilateral, according to the position of the lesion. In associated actions they work harmoniously, shewing that an intimate connexion exists between the several nuclei.

**The Third Nerve Nucleus.**—The groups of cells forming the nucleus of the third cranial nerve lie in the anterior part of the Sylvian grey matter, corresponding to the position of the anterior quadrigeminal bodies and the posterior part of the third ventricle. The nucleus is segmented, and in this respect is analogous to what is seen both in the facial and hypoglossal nuclei. The several cell-groups lie laterally as well as antero-posteriorly to each other. Various observers have described the character and arrangement of the cells (Gudden, Perlia, and others), but that given by Dr. Bruce is the one adopted here.

According to Dr. Bruce, whose terminology is consistent with the erect posture, the arrangement of the cell-groups is as follows: inferior, superior, anterior, and external groups; postero-internal and postero-external, and an unpaired median nucleus. The anterior group is composed of large cells, and extends from the lower end of the nucleus to immediately below the superior group; and commissural fibres unite the nuclei of opposite sides. Composed also of large cells is the postero-external group, having a distinct outline external to the posterior longitudinal bundle, and forming the external group. The postero-internal group is characterised by its pale colour, and the superior nucleus is formed of small cells, and lies well in advance of the other cell-groups, and external to them. This is the antero-lateral nucleus of Darkschewitseh, which lies amongst the fibres of the posterior longitudinal bundle, and is in direct relation with many of the fibres of the posterior commissure. Kölliker denies the relation of this group to the third nerve nucleus, from the facts that many of the fibres of the longitudinal bundle end in it, and that a large number of posterior commissural fibres spring therefrom.

It appears from Dr. Bruce's observations, that between the lower end of the true third nucleus and the fourth or trochlear, there is a small group of cells which he has named the inferior group. It is possible that this may correspond with that which Siemerling has described as the nucleus of the levator palpebrae muscle, and with that which Kauseh regards as the true trochlear nucleus.

The several cell-groups supply root-fibres according to their position: thus, the innermost root-fibres of the nerve spring from the median and



postero-internal groups, the outermost from the postero-external and external groups; whilst the superior group gives rise to the uppermost fibres.

A definite relation between the segments of the nucleus and the ocular muscles has been stated by many observers (Hensen and Volekers, Pick, A. Starr), but this relation is as yet quite uncertain.

The *connexions of the third nerve nucleus* are—

(i.) With the cerebral cortex through the pyramidal tracts. The exact position of these fibres is not yet definitely determined, but they probably lie in the anterior limb of the internal capsule, in close relation to the “knee.” In the crus they lie mesially, but just external, and mingling with the fibres of the fronto-pontine tract.

(ii.) With the posterior longitudinal bundles, which connect the third nucleus with those of the fourth and sixth nerves, and with the other motor cranial nuclei and probably also with the anterior horns of the spinal cords, through their continuations—the antero-lateral ground bundles.

(iii.) With the optic tracts.

Lying in the peripheral part of the Sylvian grey matter, external and dorsal to the third nerve nucleus, is a crescentic layer of large cells, giving origin to the so-called “descending” trigeminal root. These cells have normally no connexion with the fibres of the third nerve; but in some rare cases it would appear as if such a connexion were possible and might exist abnormally.

The structures through which the root-fibres pass from the nucleus to the base of the brain should be remembered in their topographical relations. Leaving the anterior part of the Sylvian grey matter, the rootlets of the third nerve pass archwise through the tegmentum cruris, the red nucleus and superior cerebellar peduncle, the substantia nigra, and the mesial portion of the pes cruris.

The nucleus of the **fourth or trochlear** nerve lies in the dorsal part of the posterior longitudinal bundles, opposite the cerebral end of the posterior quadrigeminal body. There is no sharp line of demarcation between the superior end of this and the lower end of the third nucleus; though, according to Siemerling, a distinction may be traced between them, chiefly by an alteration in the size of the nerve-cells. At the level of the trochlear nucleus and in the longitudinal bundle there is a cell-group, composed of smaller cells, which may be traced upwards and seen to merge into the third nucleus. The special value of this nucleus seems to be that it gives origin to the nerve-fibres supplying the levator palpebrae superioris muscle (Siemerling).

The trochlear root-fibres leave their nucleus and pass down in the central grey matter as far as the superior medullary velum. Here the nerves of opposite sides decussate and, passing over the superior cerebellar peduncle, course ventrally forwards towards the cavernous sinns. The position and relations of the trochlear decussation are important, as the superior oblique muscle may be paralysed from the pressure of a tumour involving the anterior end of the vermis cerebelli, the posterior quadrigeminal bodies, or the superior medullary velum. The trochlear

nucleus, from its position on the posterior longitudinal bundles, is thus closely associated with the third nucleus above and the sixth nucleus below.

**Sixth Nerve.**—The nucleus of this nerve occupies a prominent position in the dorsal part of the tegmentum pontis. It is formed of large first-type cells, whose axis-cylinder processes pass as root-fibres vertically through the tegment and pyramids, and emerge on the ventral aspect of the pons Varolii at its lower margin. The nucleus lies in a bend (genu) of the issuing root of the facial nerve, the fibres of which have no connexion with the cells of the nucleus.

The connexions of this nucleus are numerous and important. (i.) With the cerebral cortex—posterior end of the second frontal gyrus—by means of the pyramidal fibres; although, as is the case with the oculomotor nerves as a whole, the position of these fibres in the internal capsule and pes crucis is closely allied with that of the fronto-pontine tract. (ii.) By means of the posterior longitudinal bundle with the opposite third nucleus; this relation subserves the conjugate movements of the eyes (*vide* p. 516). (iii.) With the superior olivary body through its peduncle, whereby an extensive indirect connexion is established between the sixth nucleus and the auditory nerve, the corpus trapezoides, the lateral fillet, and the posterior quadrigeminal bodies. (iv.) With the flocculus cerebelli (Bruce).

**Symptoms of Ocular Paralysis.**—The muscles which move the eyeball are the four recti and the two obliques; but more than a single muscle is required to produce most individual ocular movements; for example, elevation of the globe is caused by the associated action of the superior rectus and the inferior oblique; depression by the combined action of the inferior rectus and superior oblique. The cause of this is not far to seek: the insertion of the superior rectus being lateral to its origin, its contraction produces rotation inwards as well as elevation, which is counteracted by the outward rotatory action of the inferior oblique; and the outward rotatory action of the inferior rectus is counteracted by the inward rotation caused by contraction of the superior oblique. Movement of the globe outwards and inwards is performed solely by the external and internal recti respectively; whilst conjugate movement of both globes is carried out by the associated action of the external rectus of one side and the internal rectus of the opposite side (*vide* p. 516). The two internal recti acting together produce the movement of convergence of the globes. Applying the same principles to more complicated movements we find that *rotation upwards and outwards* is effected by three muscles acting in harmony, the superior and external recti with the inferior oblique, the last-named counteracting the wheel-rotation of the superior rectus. *Rotation downwards and outwards* is carried out by the inferior and external recti, with the superior oblique to counteract the wheel-rotation of the inferior rectus. In like manner *rotation upwards and inwards* and *downwards and inwards* is brought about by the superior and internal recti and inferior

and internal recti respectively, being associated in the upward movement with inferior oblique, and in the downward movement with the superior oblique.

Paralyses of individual ocular muscles produce two series of phenomena—those of which the patient complains, and those observed by the physician. To the first class belong diplopia and erroneous projection; to the second strabismus or squint, deviation of the optic axes, and limitation of movement of the eyeballs.

(1) *Diplopia*, or double vision, is the result of strabismus. In certain positions two images are seen, the true and the false, the latter being observed in the paralysed eye. Homonymous diplopia is that in which the false image is seen on the same side as the paralysed eye. Diplopia is said to be crossed when the false image is seen on the side of the sound eye. In divergent strabismus diplopia is crossed; in convergent strabismus diplopia is homonymous.

(2) *Erroneous projection* is only apparent when the patient looks with the affected eye in the direction of the paralysed muscle. It is most marked in recent cases.

(3) *Strabismus* or squint is of two kinds: (a) concomitant strabismus from faulty innervation of an ocular muscle, and (b) paralytic strabismus from paralysis of one or more muscles. According to the deviation of the visual axes, strabismus is said to be convergent, divergent, oblique, superior, or inferior.

(4) *Primary deviation* is that which occurs in the paralysed eye on attempting to fix an object when the sound eye is covered. *Secondary deviation* is that observed in the sound eye, and occurs from overaction of the corresponding muscle, when the patient is asked to fix with the paralysed eye.

(5) *Limitation of movement* of the eyeball is in the direction of the paralysed muscle.

**Paralysis of Individual Ocular Nerves.**—The nerves supplying the eyeball and its appendages are the third, fourth, and sixth cranial, and the sympathetic nerves. The fifth nerve is the sensory nerve of the eyeball, but its relations and symptoms are described later (*vide* p. 518).

A. *The Third Nerve.*—Lesion of this nerve causes paralysis of all the external ocular muscles, except the external rectus and the superior oblique; also paralysis of the levator palpebrae superioris, the sphincter iridis, and the ciliary muscle. The symptoms, therefore, are—ptosis, inability to move the eyeball upwards, downwards, or inwards, external strabismus from overaction of the unimpaired external rectus, a wheel-rotation of the globe on asking the patient to follow the examiner's fingers downwards and outwards (from the unimpaired action of the superior oblique), dilatation and immobility of the pupil, and paralysis of accommodation. A slight protrusion of the eyeball may also be noticed. In partial paralysis any one of the individual muscles supplied by the nerve may be affected. As a general rule, there is some degree of ptosis and some interference with the pupillary reactions.



As paralysis may be due either to a nuclear or to a peripheral lesion, the symptoms vary both in degree and in extent. Ptosis is usually a common and an early symptom in both varieties. In the nuclear lesion the internal muscles may escape, while the external are paralysed.

B. *The Fourth Nerve*.—Paralysis of this nerve affects only the superior oblique muscle. As this muscle is concerned in the downward and inward movement of the globe, the diplopia is only seen in this direction; actual defect of movement is difficult to determine without the aid of the double images. The diplopia is homonymous, and the false image is lower than the true, and is inclined towards it.

Isolated trochlear palsy is infrequent. Double trochlear palsy would indicate a lesion in the neighbourhood of the anterior medullary velum, the posterior corpora quadrigemina, and the anterior end of the vermis cerebelli.

C. *The Sixth Nerve*.—Paralysis of this nerve retards the outward movement of the globe, as the action of the external rectus muscle is impaired. The strabismus is convergent; and the diplopia therefore homonymous. A slight and otherwise imperceptible weakness of this muscle may be brought out by a study of the double images; the false image lies to the side of the weakened muscle when the eyes are turned in that direction. On looking upwards and outwards, or downwards and outwards, the false image is inclined away from the true.

Unilateral abducens paralysis is not uncommon, but when coexisting with other symptoms of intracranial disease is a valuable localising sign. Owing to the long intracranial course of the nerve it is implicated in disease of the basal meninges, of the pons, of the cerebellum, and of the middle cranial fossa. Abducens palsy with contralateral hemiplegia indicates a lesion of the ventral part of the pons Varolii; but it is more common to find paralysis of the combined action of the internal and external recti muscles of opposite eyes (paralysis of conjugate movement), a symptom which points to lesion of the sixth nucleus and tegmentum pontis.

D. *The Sympathetic Nerve*.—The symptoms of a paralytic affection of this nerve from a lesion in the neck are: contraction of the pupil from palsy of the dilating fibres of the iris contained therein; narrowing of the palpebral fissure, which may give the appearance of a false ptosis, a sunken condition of the eyeball in the orbit (enophthalmos), abolition of the cilio-spinal reflex, and absence of sweating on the face on the paralysed side.

**Ophthalmoplegia**.—This consists of paralysis of either the internal or external muscles of the eye, separately or in combination, and results from lesions anywhere between the centres and the periphery.

(i.) *Cycloplegia*, or paralysis of accommodation, is a feature in paralysis of the trunk of the third nerve; it is also met with alone, chiefly as a result of diphtheria and syphilis, in which latter condition it may indicate an early degenerative change in the central nervous system. As a post-



diphtheritic phenomenon it is bilateral, and usually occurs unassociated with any other intra-ocular palsy; as a syphilitic lesion, however, it is often unilateral, and is usually accompanied by loss of the pupil light-reflex. Post-diphtheritic cycloplegia may not improbably arise from lesion of the nerve filaments within the ciliary muscle itself, although there is no direct evidence on this point. The association of cycloplegia with reflex pupillary immobility, as a symptom of syphilis, is probably due to lesion of the ciliary ganglion, as a lesion has been localised in this ganglion by Marina in tabes dorsalis and general paralysis.

(ii.) *Iridoplegia*.—The commonest form of iridoplegia is the loss of the pupillary light-reflex; if at the same time contraction on convergence is present, the condition is known as the Argyll Robertson pupil. In testing the reaction of the pupil to light, which should not be more intense than that to which the eye is usually accustomed, two actions are to be noted—the direct and the consensual pupil contraction. It is direct when light falling on one eye, the other being closed, a pupillary contraction is noted; it is consensual when, on light being thrown on one eye, the pupil of the opposite eye contracts.

The *Argyll Robertson reaction*—that is, loss of the pupillary light-reflex with pupil-contraction on convergence—may be associated either with a large or a small pupil. If the pupil be large the condition is called paralytic mydriasis or simple iridoplegia; if small it is known as paralytic myosis. A small pupil, arising from paralysis of the cilio-spinal fibres alone, may, however, contract further on the stimulus of light, and this condition is known as spinal myosis. It was held until recently, that the Edinger-Westphal or small-celled nucleus of the third nerve was the centre for the pupillary fibres. Cases, however, of total ophthalmoplegia have been recorded in which this group of cells was normal. The observations of Marina seem to place the centre for the pupillary light-reaction in the ciliary ganglion. He has observed signs of degeneration of the cells of this ganglion in a number of cases of tabes and of general paralysis, in which the pupillary light-reflex was abolished. In a case of unilateral reflex iridoplegia the ganglion was degenerated on the side of the affected eye. The view at present accepted with most favour is that the ciliary ganglion presides over the pupillary light-reflex and that the fibres reach the pupil by the short ciliary nerves.

The converse of the Argyll Robertson phenomenon, namely, the presence of the pupillary light-reflex, associated with loss of contraction on attempts at convergence, is sometimes observed.

In some cases of reflex pupillary immobility, with or without other symptoms of tabes dorsalis, anaesthesia over the distribution of the trigeminal nerve has been found. This points to a sclerotic lesion, either in the trunk of the fifth nerve, or more probably in the spinal trigeminal root in the medulla oblongata.

*The Motor Pupillary Fibres*.—The peripheral course of the pupil-contracting fibres is through the rootlets of the third nerve, the trunk of the nerve, the ciliary ganglion, and the short ciliary nerves. The course

of the pupil-dilating fibres is more circuitous: they pass through the pons Varolii, medulla oblongata, and cervical region of the spinal cord, to issue by the anterior root of the first and second dorsal nerves and to be conveyed in the cervical sympathetic, the ophthalmic branch of the fifth, and the long ciliary nerves to the iris.

From experiments upon the fifth nerve and its intra-medullary roots, it is evident that the pupil-dilating fibres pass chiefly in the gelatinous substance of Rolando or adjacent tissue; for section of the so-called ascending trigeminal root and destruction of the tubercle of Rolando are invariably followed by contraction of the pupil on the side of lesion. That the sensory root of the trigeminus between the side of the pons and the Gasserian ganglion also contains pupil-dilating fibres is clear from the fact that on cutting the root contraction of the pupil is observed.

(iii.) *Ophthalmoplegia Interna*.—This name is given to a condition in which all the internal ocular muscular mechanisms are paralysed. It presents the clinical features of paralysis of accommodation, mydriasis, and pupillary immobility. The condition may be unilateral or bilateral; or it may be complete on one side and partial on the opposite side. It may or may not be associated with paralysis of the external ocular muscles. When these symptoms occur alone, the lesion is probably in the ciliary ganglion, or in the roots or trunk of the third nerve.

(iv.) *Ophthalmoplegia Externa*.—Under this name are included those forms of ocular paralysis in which more than one external ocular muscle is paralysed. Hence there exists a large number of ocular palsies due to lesions in various situations, of different nature, and arising from many causes, both acute and chronic. The form, however, which may be taken as the standard or type is that arising from chronic degeneration of the cells of the oculomotor nuclei;—*chronic nuclear ophthalmoplegia*. This condition presents many clinical varieties; it may exist alone as a pure ophthalmoplegia for a number of years, or it may be associated with a like degeneration of the bulbar nuclei, or with tabes dorsalis. In a complete case all movements of the external ocular muscles are paralysed, with or without drooping of the upper eyelid. In partial cases diplopia is troublesome. A common symptom also, and probably characteristic of nuclear affection, is an alternating ptosis, sometimes more marked in one eye, sometimes in the other; there is also a tendency to remission and exacerbation.

Both eyes are usually affected, but not always to the same extent; and, in the pure cases, the internal ocular muscles and the reflex action of the iris to light are unaffected. Weakness of the orbicularis palpebrarum has been observed in cases of nuclear ophthalmoplegia. When this is present an extensive nuclear degeneration may be diagnosed. Although in these cases the lagophthalmos met with in facial paralysis is not seen, yet by the examiner's finger the upper lid may be raised against resistance more readily than is possible in a healthy condition.

A form of ophthalmoplegia, differing from the above in its method of onset, is due to *polioencephalitis superior* (Wernicke) (*vide* Vol. VIII.). In this

there is an ophthalmoplegia of sudden origin, not uncommonly associated with symptoms, such as delirium, somnolence, and sometimes optic neuritis. In some cases the symptoms point to a coexistent implication of the grey matter of the floor of the fourth ventricle and of the anterior horns of the spinal cord. These cases, whether the symptoms be limited to the oculomotor nerves or shew a simultaneous affection of the bulbar and spinal grey matter, are often fatal; and post-mortem examination has revealed hæmorrhagic extravasations in the grey matter around the Sylvian aqueduct, and in the walls of the third ventricle with vascular distension and thrombosis; whilst a similar pathological condition has been observed in the bulbar and spinal grey matter. Although many of these cases have a similar causation to acute poliomyelitis, others are more especially due to chronic alcoholism, influenza, diphtheria, or lead.

But there are cases of acute nuclear ophthalmoplegia, occurring without such well-marked general symptoms, which do not present any evidence of implication of the central grey matter elsewhere. Such cases are not rapidly fatal, and many recover. In these cases the causal agent is some infection—syphilis, diphtheria, influenza, and others still undetermined. This condition is similar to what occurs elsewhere in the central nervous system. An acute inflammatory lesion may occur in the cerebral cortex, giving rise to hemiplegia, more especial in children, in the medulla where it occasions a form of acute bulbar paralysis, and in the spinal cord, where it occurs as acute poliomyelitis.

**Varieties of Ophthalmoplegia.**—1. *Cortical Ophthalmoplegia (so-called).*—Ophthalmoplegia, defined in its proper sense as impairment of the movements of the eyeballs in all directions, does not occur in purely cortical lesions. As an experimental result of destructive lesion of the area in which stimulation causes deviation of both eyeballs to the opposite side, or of extirpation of the frontal lobe in monkeys, and in some cases of disease of this region in man, temporary paralysis of conjugate movement of the eyes to the side opposite the lesion has been observed; but both frontal lobes, containing the excitable areas for such ocular movements, may be completely extirpated without any evidence, other than temporary, of defective conjugate movements.

2. *Subcortical ophthalmoplegia*, or paralysis of the ocular movements from disease affecting the fibres between the cortex and the oculomotor nuclei, as in the so-called cortical form, is unknown, except a temporary paralysis of conjugate movement which occurs as an early and fleeting effect of hæmorrhage within, or in the neighbourhood of, the internal capsule and the basal ganglia.

3. *Nuclear ophthalmoplegia* has already been described.

4. *Infra-nuclear (or basal) Ophthalmoplegia.*—Under this name are included those ocular palsies due to a lesion situated between the oculomotor nuclei and the eyeball.

A lesion which involves the third nerve and the crus cerebri produces one form of alternate paralysis—paralysis of the third nerve on one side and of the limbs on the opposite side (Weber's symptom). This paralysis



may also arise from lesion within the substance of the crus (intra-peduncular); or outside it, in connexion with the membranes. The intra-peduncular form is usually associated with hemichorea or hemi-athetosis, cerebellar instability, and ataxia.

The causes of such palsies are tuberculous or syphilitic inflammation or new growths of the basal membranes, syphilitic obliterative arteritis of the basilar artery or its branches, meningitis in the neighbourhood of the sphenoidal fissure, and thrombosis of the cavernous sinus.

5. *Orbital Ophthalmoplegia*.—The causes of this form of ophthalmoplegia are fractures through the sphenoidal fissure, periostitis, tumours, and inflammatory lesions within the orbital cavity. With these lesions the ophthalmic branch of the fifth rarely escapes, and the optic nerve itself is not uncommonly implicated, especially when the lesion is in the neighbourhood of the sphenoidal fissure and optic foramen. The association of such paralytic phenomena with proptosis suggests an orbital affection, as distinguished from one in the neighbourhood of the cavernous sinus or sphenoidal fissure.

6. Rare forms of ophthalmoplegia are found in association with migraine, myasthenia gravis, and hysteria.

**Associated Paralyses.**—*Paralysis of Convergence*.—Paralysis of the convergent movements of the internal recti muscles may occur, while their associated movement with the external recti is preserved. With the palsy of convergence there is loss of the associated pupil-contraction, but the pupillary light-reflex is retained. Paralysis of convergence is associated with paralysis of accommodation. In palsy of convergence the unopposed action of the external recti muscles may occasion a slight bilateral divergent strabismus. Paralysis of convergence, without loss of the other muscular movements supplied by the third nerve, is due to disease of the centres, but it is not yet known what group of cells in the third nerve nucleus presides over this function.

*Paralysis of Conjugate Movement*.—The eyeballs are normally moved to either side by the associated action of the internal and external recti muscles. In certain diseases of the central nervous system this normal action may be impaired; on the one hand, the eyes may be forcibly deviated to one or other side from tonic spasm of the associated muscles; or, the patient may be unable to turn the eyes to one or other side owing to paralysis of the associated mechanisms. The former condition is due to an irritative lesion above the centre in the pons Varolii, the latter is caused by destructive lesion of the centre in the pons.

The sixth nucleus is the pontine centre for conjugate movement. This nucleus has an extensive connexion with adjacent structures which appear to be associated with the movements of the eyes. Thus, it is directly connected with the superior olivary body, with the flocculus cerebelli, and through the nucleus of Deiters it has an indirect connexion with the middle lobe of the cerebellum and the spinal cord. From the sixth nucleus, by way of the posterior longitudinal bundle, fibres pass to a group of cells in the third nucleus which supply the internal



rectus muscle of the opposite side. That this group of cells is distinct from that which innervates the internal rectus muscle for movements of convergence is probable from the fact that palsy of convergence may exist without palsy of conjugate movement.

A lesion, therefore, in order to cause palsy of conjugate movements must be either in the course of the fibres above the sixth nucleus, or involve the nucleus itself. The latter is the commonest situation.

Sometimes associated with this paralysis is facial palsy on the same side. The cause of this association is apparent when it is borne in mind that the sixth nucleus lies in the "knee" of the facial nerve-root.

It is still doubtful how far a lesion limited to the posterior longitudinal bundle may cause palsy of conjugate movement. No such limited case has been recorded in human pathology.

Of *other associated ocular movements* may be mentioned a pupillary contraction which is stated to occur on forced closure of the orbicularis palpebrarum. Gifford noted in some cases, more especially in these associated with blindness, that on forced contraction of the lids,—as, for instance, when an attempt is made to close them against resistance,—a contraction of the pupil takes place with the normal upward movement of the globe. It appears that this reaction occurs independently of convergence or accommodation, and points to a close relation between the centres of pupillary contraction and closure of the lids. Some fibres of the third nerve may pass directly to the palpebral portion of the orbicularis palpebrarum muscle by way of the supraorbital branch of the fifth nerve.

An associated action has been described between certain movements of the lower jaw and the upward movement of the upper eyelid. Numerous cases have now been recorded, and according to Sinclair may be divided into three groups: first, cases of one-sided congenital ptosis, in which the drooping eyelid is raised when the mouth is opened, and when the jaw is directed to the opposite side; secondly, cases of one-sided congenital ptosis, in which the lid is raised when the jaw is depressed only; and, thirdly, those cases in which elevation occurs only with lateral movement of the jaw: other cases again have been noted in which no ptosis was observed, but in which the upper lid jerked when the jaw was moved. In the recorded cases the abnormal congenital condition leading to ptosis may be associated with an abnormal connexion between the third nerve nucleus and the descending trigeminal root.

A rare association is that between the internal rectus and the levator palpebrae muscles on the same side, which contract and relax together. An associated movement has been described in some cases of paralysis of one external muscle, in which movement inwards of the affected eye is associated with contraction of the orbicularis palpebrarum and retraction of the globe (Sinclair).

**Causes of Ocular Paralysis.**—The causes of ocular palsies have been incidentally mentioned in the descriptions of the several forms just related. A short summary may, therefore, be appended. Paralysis of

the third, fourth, and sixth nerves may be due to: (1) Injuries of the base of the skull, periostitis, and local orbital diseases; (2) Within the skull to new growths and inflammatory affections of the basal meninges. They may also be affected by a general increase of the intracranial pressure; (3) Toxic causes, such as diphtheria involving the nuclei of origin; (4) New growths or localised vascular lesions within the pons and *circa cerebri* affecting the nuclei of origin; (5) As part of a general infective or toxic condition such as poliomyelitis; (6) In the course of some chronic nervous disorders, such as tabes dorsalis and disseminated sclerosis; (7) In association with migraine, myasthenia gravis, and hysteria; (8) Congenital ocular paralyses.

The treatment of ocular palsies is conducted according to general principles. As peripheral ocular palsies are almost invariably due to specific causes (syphilis, rheumatism, diphtheria, and other toxic agents), the respective specific remedies in common use should be administered. Local remedies, such as leeching or blistering the temples or forehead, are often of the greatest service, more especially in the early stages, and when the palsy is accompanied by headache, which is not uncommonly the case.

In the acute ophthalmoplegias arising from nuclear causes the same specific remedies may be applied as in the peripheral cases. In the chronic degenerative forms not much benefit is likely to be obtained by drugs. In these cases the local application of electricity, chiefly in the form of weak galvanic currents, has been recommended, and in some cases has seemed to be of value; but it should be borne in mind that a tendency to remission is one of the features of the disease, and that the degenerative process may be spontaneously arrested for a longer or a shorter time.

**THE TRIGEMINAL NERVE.—Anatomy.**—When seen at the base of the brain this nerve consists of two divisions, a large sensory and a small motor root.

(i.) The *sensory root* may be readily traced amongst the fibres of the middle cerebellar peduncle into the lateral part of the tegmentum pontis. Here some fibres pass directly into the so-called sensory nucleus (*convolutio quinti*), which is nothing else than the expanded proximal termination of the *substantia gelatinosa* Rolandi. The remainder of the division may be followed through the pons Varolii and medulla oblongata, in the distal part of which it forms the layer of white matter covering the gelatinous expansion or tubercle of Rolando. The fibres composing this root are the axis-cylinder processes and collaterals of the cells of the Gasserian ganglion. They terminate in the medulla oblongata in the gelatinous substance, which lies on the mesial surface of the spinal root as far down as the upper cervical nerves.

Section of the sensory division between the Gasserian ganglion and the brain, or its involvement by disease, is followed by degeneration and atrophy of the fibres entering the so-called "sensory nucleus," by sclerosis

of the spinal root, as far as the second cervical nerve, and of the fibres which pass from this root through the gelatinous substance into the posterior horn of grey matter.

(ii.) *The Motor Root.*—The motor root consists of fibres issuing from the motor nucleus and those from the descending or “trophic” root.

The cells of the motor nucleus consists of large, multipolar, first-type cells, which send their axis-cylinder processes directly into the motor root, and form the *efferent* fibres of the nucleus.

The descending or “trophic” root of Merkel is now regarded as a portion of the motor division of the trigeminal nerve. There is no proof that it has any trophic functions upon the eye. Most probably it supplies motor fibres for the tensor palati and tensor tympani muscles (Kölliker).

**Paralysis of the Fifth Nerve.**—The symptoms of paralysis of the trigeminal nerve fall into two sets, according as the motor or sensory branches of the nerve are implicated.

*Motor Paralysis.*—Paralysis of the *motor branch* is indicated by weakness and atrophy of the muscles of mastication. The feebleness or inability to contract may be detected manually in the case of the temporal and masseter muscles; whilst unilateral loss of power in the pterygoid muscles is shewn by the deviation of the lower jaw to the paralysed side when the mouth is opened, and by inability to move the jaw to the non-paralysed side.

As Sir W. Gowers states, there is no sign of the paralysis of the tensor tympani and tensor palati muscles in affections of this nerve; nor, likewise, is there any evidence of paralysis of the mylohyoid and anterior belly of the digastric, although these muscles are probably innervated through the motor fifth.

The *causes* of this paralysis are similar to those affecting the other motor cranial nerves. Thus, the motor nuclei of the nerves may be affected in the chronic form of progressive bulbar palsy. Usually this is a late phenomenon, but it has been observed in the early stages, more especially in association with primary affection of the oculomotor nuclei.

The roots of the nerve are involved in the pathological conditions affecting the dura mater of the base, alone or in association with adjacent nerves, chiefly the oculomotor. Unilateral trigeminal palsy, with or without implication of the auditory nerve on the same side, and associated with symptoms of cerebellar disease, is characteristic of tumour of the cerebello-pontine angle or of the auditory nerve or of the base of the skull.

*Sensory Paralysis.*—Sensory paralysis consists of loss or impairment of the epicritic and protopathic sensibilities over the cutaneous distribution of the nerve. The deep sensibility is lost when there is total abolition of cutaneous sensibility (Davies.) The mucous membrane of the tongue becomes dry, furred, and covered with the debris of food. The inside of the cheek may shew ulcerated patches where it has been unintentionally bitten during mastication. The mucous membrane of the nose is



dry, and the sense of smell is impaired. Trophic ulcers may or may not be seen upon the cornea. The pupil on the side of the lesion is smaller than the normal one.

Herpes may be occasionally observed over the distribution of the nerve, but is usually confined to the supraorbital, nasal, and supra-trochlear branches and the cornea.

*Sensory Distribution.*—There is only slight overlapping between the distribution of the trigeminus and the cervical plexus. The areas of epicritic and protopathic loss are almost identical. Excluded from the area of anaesthesia following removal of the Gasserian ganglion are the external auditory meatus and the skin over the major portion of the lower jaw. Included in the sensory trigeminal distribution are the mucous membranes of the nostril, one-half of the tongue as far as the circumvallate papillae, the anterior pillar of the fauces, and half the soft and hard palates and the upper lip (*vide* also p. 542).

Anaesthesia over the distribution of the nerve on one side, with or without coexistent affection of the motor root, indicates a lesion of the root of the nerve between the Gasserian ganglion and the surface of the pons Varolii. In cases of this character symptoms of cerebellar disease may be present, pointing to an affection, usually tumour, of the middle cerebellar peduncle, involving the trigeminal roots.

Should the spinal root in the pons be involved, facial anaesthesia will be present on the side of the lesion, and probably motor and sensory paresis of the body and limbs on the opposite side.

The presence of trigeminal anaesthesia on the same side as that of the body and limbs points to a lesion above the entrance into the pons of the sensory root of the fifth nerve; and, according to the associated phenomena, it may be placed either in the upper part of the pons, the crus cerebri, or the posterior part of the internal capsule.

The sensory corticipetal fibres would appear to run with those from the body and limbs in the tegmentum pontis and crus upon the opposite side, or pass into the ventral portions of the optic thalamus from which they are transmitted to the cerebral cortex.

The symptom known as *neuro-paralytic keratitis* is not an essential accompaniment of paralysis of the sensory root. Both experimental and clinical results support the view that it is a symptom of irritation and not of paralysis of the sensory division. This question is discussed elsewhere (pp. 84, 332).

**Treatment.**—Little need be said about the treatment of paralysis of the fifth nerve. In the majority of cases the internal administration of specific remedies with local counter-irritation is all that can be done medicinally.

In paralysis of the muscles of the jaw from lesions of a degenerative nature, the hypodermic injections of strychnine are to be recommended, in conjunction with local electrical treatment (faradism or galvanism as the case may require), according to the reaction of the muscles.

For an account of trigeminal neuralgia see p. 540.



**THE FACIAL NERVE.**—The facial nerve is a mixed nerve, the motor division being the *portio dura*, and the sensory division the *pars intermedia* or nerve of Wrisberg. The *nucleus of origin* of the motor facial nerve is situated in the ventral portion of the tegmentum pontis, immediately dorsal to and outside the superior olivary body. As in the case of both the third and hypoglossal nuclei it is segmented.

The nerve-roots pass dorsally, in a series of fasciculi, towards the floor of the fourth ventricle; on reaching which position they are collected in a compact bundle, to be seen mesial and somewhat dorsal to the sixth nucleus. The root-fibres, which hitherto have held a vertical course, now pass horizontally under the floor of the ventricle, as far as the upper (proximal) end of the sixth nerve nucleus. Here they turn obliquely outwards, and passing through the tegmentum and transverse fibres of the pons, reach the surface in a position between the trigeminal and abducens nerves, and ventral to the auditory nerve.

The nucleus is connected with the cortex cerebri by fibres which descend in close relation to the fibres of the other cranial nerves. Bechterew places them immediately posterior to the "knee" of the internal capsule; in the crus cerebri they form the innermost of the bundles of the pyramidal system, and lie immediately external to the fronto-pontine tract, which is the most mesial of the bundles in this region. Spitzka observed degeneration of this bundle after a destructive lesion of the cerebral cortex involving the facial and hypoglossal areas.

A direct connexion between the hind part of the third nerve nucleus and the issuing root of the facial nerve to which prominence was at one time given, has not received the corroboration and support of fuller investigation. The experiment of Mendel supported this contention, and some clinico-pathological evidence was advanced in its favour in the first edition of this *System* (1899, Vol. VI. pp. 780, 796).

A direct connexion is stated to exist between the hypoglossal nucleus and the facial nerve—a relation originally pointed out by Lockhart Clarke. Anatomical evidence of this is so far wanting, but some clinical facts lend support to the view.

*The Sensory Root or Nerve of Wrisberg.*—The observations of Martin and His shewed that the fibres of this nerve arose in the ganglion geniculi facialis, and, according to Duval, belonged entirely to the facial nerve, and formed the fibres of the chorda tympani. The cerebral termination of the nerve remains obscure: His traced it into the "solitary bundle" or ascending vago-glossopharyngeal root, a connexion recently corroborated by Ramsay Hunt.

The functions of this nerve are discussed with the sense of taste on p. 525.

**Facial Paralysis.**—This is one of the commonest forms of cranial nerve palsy, and arises both from central and peripheral causes. Facial palsy of central origin will be considered on p. 523, as it shews certain features by which it may be distinguished from the more common peripheral type. By far the commonest variety of this is the so-called "rheumatic" facial

paralysis, caused in the majority of cases by cold. At least 88 per cent of the cases arise from this cause. It is probably an infective neuritis which has a seasonal incidence, being more common during the months of April, October, and November. Other causes of facial palsy of the peripheral type are basal syphilitic meningitis, and tumours of the cerebello-pontine angle.

The pathological change underlying the peripheral form of facial palsy is a parenchymatous neuritis, with disintegration of the medullary sheaths. It is most apparent in the peripheral distribution of the nerve, and at the distal end of the Fallopian canal. There is not sufficient pathological evidence on which to base the statement that in the rheumatic form of facial palsy the nerve is compressed by inflammatory material, either in the Fallopian canal or at its issue from it. The pathological evidence locates the change chiefly in the nerve branches distributed over the face, and in the outer part of the Fallopian canal; and the pathological state of the nerve is a parenchymatous and not an interstitial inflammation.

Regarding other aspects in the pathology of facial paralysis, there are to be noted the forms associated with (a) chronic degenerative atrophy of the cells of the facial nucleus; (b) implication of the nerve-roots by lesions situated in the tegmentum pontis; (c) destruction of the nerve-roots by gummatous or other new growths involving the dura mater of the base of the skull.

The *symptoms* of a complete facial palsy are so characteristic that a detailed description of the condition is unnecessary. There is loss of movement over the whole of the affected side of the face, and when the patient is requested to close the eyes, the eyeball on the paralysed side is seen to roll upwards, owing to the absence of descent of the upper lid. Whistling is impossible, and the tongue, when protruded, may give a false impression of deviation to the paralysed side. Food collects between the jaw and the cheek; and in drinking, the fluid may run out at the angle of the mouth. Taste may or may not be abolished on the anterior two-thirds of the tongue. In mild cases, characterised by slight facial palsy and quantitative diminution of the faradic excitability, taste may not be affected at all, indicating a limitation of the affection to the peripheral distribution of the nerve; whereas in more severe cases taste is lost by an extension of the neuritis into the Fallopian canal towards the geniculate ganglion with implication of the chorda tympani nerve.

In facial palsy from lesion of the nerve-trunk paralysis of the soft palate does not occur. The association of these symptoms, which is commonly described, is due to simultaneous affection of the facial and vago-glossopharyngeal nerves.

Hearing is often implicated. Should the lesion causing the facial palsy be middle-ear disease, air-conduction of sound may be abolished; but in cases in which the nerve to the stapedius muscle is involved, without otitis media, an increased sense of hearing may exist, especially to musical sounds.

Cases are met with in which no such complete invasion of the facial muscles is detected. Many cases of facial palsy are incomplete, and it is well known that the frontalis and orbicularis palpebrarum are especially retentive of faradic excitability—a fact which may indeed suggest the possibility of their further innervation directly from the third nerve nucleus, through the connexion which exists between the third and fifth nerves at the sphenoidal fissure. It is a common observation that the oculo-facial group recovers its electrical irritability earlier than the other facial muscles.

The escape of the orbicularis oris in the cases of congenital facial palsy recorded by Schultze and Bernhardt, tells in favour of the innervation of this muscle from the hypoglossal rather than from the facial nucleus—a fact which is also emphasised by the unique case described by Sir W. Gowers, in which the orbicularis oris escaped when the facial nucleus was affected by acute poliomyelitis.

In the ordinary type of the disease recovery usually occurs, but in the severer forms *secondary contracture* ensues. In repose this may induce a false appearance of weakness on the healthy side. In these cases attempts to close the eyelids will result in partial failure and in an over-action of the levator anguli oris, so that the mouth will be pulled over to the paralysed side, but on shewing the teeth the mouth is pulled to the non-paralysed side.

**Varieties of Facial Paralysis.**—(i.) *Cortical and Subcortical Facial Palsy.*—Paralysis of the face follows destructive lesions of the cerebral cortex at the lower end of the ascending frontal gyrus and of the fibres which pass from this centre to the facial nucleus in the pons Varolii. The lesion may be either on one or on both sides of the brain.

The characteristic feature of cerebral facial paralysis lies in the greater implication of the lower facial muscles, the upper being relatively intact. It is a mistake, however, to suppose that the oculo-facial group is not weakened in this form; although the eyelids may be closed voluntarily, yet on the side of the paralysis the patient is usually unable to resist attempts to open them. Should there be weakness on both sides, as is seen in the so-called *pseudo-bulbar paralysis*, the weakness of the oculo-facial group is bilateral, but it is not complete.

In the cerebral form, also, although the voluntary movements of the mouth are paralysed on one side, the emotional are as a rule retained; in the peripheral type both forms are abolished. Facial weakness, as described from cortical and subcortical causes, does not occur alone, being associated with paresis of the tongue movements and defective articulation, and paralysis of the limbs on one or both sides. The electrical irritability of the muscles is unchanged, or at the most presents a slight general quantitative diminution.

(ii.) *Nuclear paralysis* is usually of the chronic type and rarely occurs alone, being found in association with atrophic palsy of the bulbar and limb muscles. The electrical reactions are of a quantitative rather than a qualitative character.



(iii.) *Root Paralysis*.—The facial nerve is not uncommonly involved in disease (gumma, tubercle, etc.) of the dura mater of the base of the skull, with or without associated paralysis of the auditory nerve; in such cases the symptoms are those of a palsy of the peripheral type. The condition is not uncommonly bilateral, and gives rise to *diplegia facialis*. Other cranial nerves may be affected simultaneously; more especially the auditory, which in the subdural space lies immediately superior and dorsal to the facial. Cases of *diplegia facialis* with bilateral deafness are due to bilateral tumours in the cerebello-pontine angle, to gummatous meningitis, or to fracture of the base of the skull.

(iv.) Facial palsy of the peripheral type is observed in diphtheritic, alcoholic, and lead neuritis. Weakness of the facial muscles is also seen in the myopathies and myasthenia gravis.

Simultaneous bilateral otitis media has been known to cause peripheral *diplegia facialis*; also the application of the forceps at the time of birth.

The **prognosis** of facial paralysis is based upon—first, the seat of the lesion; and, secondly, in peripheral cases upon the electrical reactions. In the nuclear variety the prognosis is grave, because the facial weakness is merely an element in a degenerative process occurring throughout the bulbo-spinal centres.

If the palsy be associated with disease in the subdural space, the prognosis also is bad, as it is seldom that the affection remains limited; although, if it be of a syphilitic nature, a certain amount of recovery may take place under suitable treatment.

Of the purely peripheral forms, that due to disease of the middle ear is the least satisfactory; only in rare instances do these forms shew any marked improvement, although the aural disease may be carefully treated and cured. Secondary contracture of the muscles on the paralysed side is, in this form, not uncommon.

In the peripheral forms of rheumatic nature, already shewn to be by far the commonest variety of facial palsy, an *electrical examination* is essential in order to form a satisfactory prognosis. If from a week to ten days after the onset of the paralysis there is no quantitative diminution, but rather an increase to faradic stimulation, recovery will take place in three or four weeks. If at about the same time after the onset the faradic irritability be distinctly lessened quantitatively, recovery is likely to take place in from six weeks to two months. Should the faradic excitability be entirely lost in seven to ten days after the onset, recovery is likely to be delayed for three months. In this case, in addition to the loss of faradic reaction, there is likely to be qualitative galvanic alterations, seen in the reaction of degeneration. If the faradic excitability remain in abeyance three, four, or more months after the onset, the prognosis as to recovery should be guardedly given. In such cases the onset of secondary contracture is highly probable.

**Treatment**.—This is, for all practical purposes, limited to the purely peripheral type of palsy. In the mildest forms, characterised by a slight



diminution of the faradic excitability of the muscles on the weakened side of the face, little or no active treatment is required; the application of a mustard leaf or small fly-blister behind the ear and the prevention of fresh exposure to cold are all that is needed, as recovery will take place in from three weeks to one month.

In the more severe forms of facial palsy, especially in those associated at the outset with considerable pain, care ought to be taken in the use of counter-irritants. I have seen a case in which the injudicious use of croton oil, as a counter-irritant, provoked most intense cellulitis over the parotid region; in such cases the careful use of small mustard-leaves, repeated several times, may be of greater service than the application of a cantharides blister.

In cases arising from disease of the middle ear, the treatment of this latter condition is absolutely essential before any measures may be taken for the relief of the paralysed side of the face. On the whole such cases are distinctly unsatisfactory, especially if the ear disease be of long duration; for the nerve becomes so irretrievably disorganised as to obliterate all means of reorganisation.

As regards the use of electricity in facial palsy, the variety to be adopted is that to which the muscles respond. As long as faradic excitability is absent the galvanic current may be used with advantage.

Massage of the facial muscles in all cases is of value in preserving the muscular nutrition and the lines and contour of the face and to prevent contracture of the paralysed muscles. In cases incurable by other means, anastomosis of the facial with the hypoglossal or spinal accessory nerve has been practised.

**The Sense of Taste.**—In addition to the tongue, the mucous membranes of the soft palate and palatine arches subserve the sense of taste. Three nerves preside over this function: (a) the chorda tympani for the anterior two-thirds of the tongue; (b) the glossopharyngeal for the posterior third; (c) a branch from Meckel's ganglion for the soft palate and palatine arches. The taste fibres for the anterior two-thirds of the tongue are distributed in the lingual branch of the fifth nerve, from which they pass into the chorda tympani and thence into the geniculate ganglion of the facial nerve. Those distributed from Meckel's ganglion probably reach the facial nerve through the great superficial petrosal and Vidian nerves. The taste fibres of the posterior third of the tongue may or may not be wholly transmitted to the brain by the roots of the glossopharyngeal nerve. Some of the fibres may possibly travel through the nerve of Jacobson and the small superficial petrosal to the otic ganglion.

The much-discussed question as to how the fibres for taste are transmitted to the brain has received important statistical evidence from the studies of the cases in which the Gasserian ganglion has been removed for trigeminal neuralgia. Both Cushing and Morriston Davies have shewn that after this operation taste is only exceptionally impaired or lost. Out of 39 cases of excision of the Gasserian ganglion, taste was unaffected in 33, impaired in 4, and lost in 2. The cases in which taste was impaired

may be explained by mechanical injury to the geniculate ganglion or to the superficial petrosal nerve, or to a possible variation in the course of the taste fibres in some persons. It may therefore be accepted that, with a few unimportant exceptions, taste fibres are not transmitted through the sensory root of the trigeminal nerve. What therefore is the path of the taste fibres? It is now conceded that the *pars intermedia*, or nerve of Wrisberg, is the sensory root of the facial nerve, and through it pass the fibres from the geniculate or sensory ganglion of the seventh nerve to the brain. Herpetic lesions of the geniculate ganglion have been followed by degeneration in the nerve of Wrisberg, which has been traced into the *fasciculus solitarius*, in which structure the glossopharyngeal roots also in part terminate (Ramsay Hunt). Although clinical proof of the passage of the taste fibres by the sensory root of the seventh nerve is not yet established by a large number of observations, yet there is much in favour of this being the root by which the fibres of taste reach the brain.

**THE EIGHTH NERVE.**—The eighth nerve-trunk, having arrived at the side of the pons Varolii, divides into two nerve-roots, one of which passes mesial to the restiform body, the other dorsal and external to it; the former is the anterior, mesial, or *vestibular* root, the latter being the posterior, lateral, or *cochlear* root. Upon the cochlear root is the anterior or accessory auditory ganglion. In the dorso-lateral part of the pons there lie two other auditory nuclei, the dorsal or chief auditory nucleus, and the external or Deiters' nucleus. The eighth nerve is composed of two distinct nerves, having separate origins, separate terminations, and different functions.

**1. The Vestibular Nerve.**—The fibres of this nerve, arising in the lining membrane of the semicircular canals, pass in the trunk of the eighth nerve, and enter the pons Varolii between the restiform body and the ascending trigeminal root. Some of the fibres terminate in Deiters' nucleus, and others pass into the dorsal nucleus. It is not clear that any pass directly into the so-called descending auditory bundle. The chief part of the vestibular root passes on to the nucleus vestibularis, which lies at the outer angle of the fourth ventricle.

The end-nuclei of the vestibular nerve are therefore the vestibular nucleus, Deiters' nucleus, and the dorsal auditory nucleus. These nuclei are connected with the cortex of the middle and lateral lobes of the cerebellum by a number of cerebellar afferent fibres. The nucleus of Deiters has also a connexion of an efferent character with the vermis cerebelli. These fibres pass from the several vestibular end-nuclei into the tegmentum pontis; others pass into the posterior longitudinal bundle, whilst others cross the raphe and appear to enter the lateral fillet.

A third connexion of Deiters' nucleus, and one of much importance, is with the antero-lateral tract of the spinal cord. Experimental destruction of Deiters' nucleus has been followed by a tract of degeneration passing downwards through the medulla into the antero-lateral periphery of the spinal cord—the vestibulo-spinal tract.

Two other connexions of Deiters' nucleus have also been described: one with the inferior olivary body, and the other with the nucleus of the sixth nerve. The chief function of Deiters' nucleus is what Deiters originally stated, namely, an internode in a great cerebellar spinal system.

*Physiology of the Vestibular Nerve.*—This nerve is the path by which impulses from the semicircular canals reach the brain, more especially the cerebellum. Lesions of the semicircular canals and the vestibular nerve in animals are followed by profound disturbances of equilibration. After experimental section of the nerve, the animal rolls many times in succession towards the side of lesion. These effects are of a temporary character, the animal eventually regaining its equilibrium, though never completely. Similarly in man, lesions of the labyrinth and of the vestibular nerve are associated with vertiginous attacks and disturbance of equilibration. According to Prof. Sherrington, the labyrinth is the "receptor organ" of the head segments, and with other receptive organs in the limbs and trunk forms a proprioceptive system, the head ganglion of which is the cerebellum.

2. *The Cochlear Nerve.*—The fibres of this, the second division of the auditory nerve, arise as axis-cylinder processes of the cells of the cochlea, and pass in the trunk of the nerve to the anterior or accessory nucleus (auditory ganglion) situated outside the medulla oblongata on the trunk of the nerve. Here many of the fibres terminate in end-tufts around the ganglion-cells, whilst others pass dorso-externally over the restiform body to terminate in a similar fashion in the so-called *tuberculum acusticum*, which lies on the dorso-lateral aspect of the medulla.

The cochlear fibres differ from the vestibular in two respects: first, they are of smaller size; and, secondly, they receive their medullary sheaths at a later date, so that on a section of the nerve the two sets of fibres may be distinguished.

There is reason to believe that the auditory tubercle and the accessory ganglion are parts of the same structure; and as the fibres of the cochlear nerve end therein, the term *cochlear end-nucleus* may be appropriately given (Kölliker). And in this relation also lies the explanation of the fact that section of the auditory nerve-trunk, as it enters the internal auditory meatus, is not followed by degeneration beyond the cochlear nuclei just described, or the vestibular end-nucleus to which reference has already been made.

The central connexions of the auditory ganglion are of great importance, as they form the *central auditory tract*. As a result of destruction of the auditory ganglion, degeneration may be traced through the fibres of the corpus trapezoides, across the raphe, into the lateral fillet of the opposite side. In connexion with the degeneration of the trapezoid body, the mesial of the two portions into which the superior olivary bodies are divided shewed extensive degenerative changes on both sides. Degeneration was followed through both lateral fillets, more extensive on the side opposite the lesion, through the tegmentum cruris and into the internal geniculate body. The posterior corpora quadrigemina appeared to be



ganglia accessory to the central auditory tract, rather than to be situated in it. There is reason to suppose that the internal geniculate body stands in a relation to the auditory tract similar to that of the external geniculate body and pulvinar thalami to the visual fibres. From the internal geniculate body fibres pass to the superior temporal gyrus. It is not clear whether there is a direct connexion between the auditory ganglion and the cortex, or whether the connexion is indirectly through the internal geniculate body.

Situated on the external surface of the crus cerebri is a bundle of fibres known as the "bundle of Turck," or "lateral pontine system." This tract degenerates downwards after a destructive lesion of the first temporal gyrus. From this it is apparent that the temporal lobe has a double connexion with the hind-brain: one, a projection system, from the temporal gyri to the pons Varolii; the other, an afferent system, passing from the accessory auditory ganglion by way of the trapezoid body, the lateral fillet, and internal geniculate body.

*Cortical Auditory Centre.*—Dr. A. W. Campbell has shewn that in connexion with the primary auditory centre, which occupies the gyri of Heschl in the Sylvian fissure, there is a higher or audito-psychical centre in the posterior part of the first temporal convolution. In this centre, in right-handed persons on the left side of the brain, the auditory speech-centre is situated. Lesion of this area is associated with word-deafness, or the loss of power of interpreting spoken language, and the power of recalling words and names.

**Symptoms of Nerve Deafness.**—When a person complains of deafness, it is essential to ascertain, in the first instance, whether this symptom be due to obstruction in the external auditory meatus, to disease of the middle ear, or to causes impairing the reception of sound by the internal apparatus and its conduction by the auditory nerve and central nervous mechanisms.

In many cases the history of the onset of deafness is of value in directing the physician's attention to the apparatus affected; and if no objective sign is obtained of the existence of external or middle ear disease, the following symptoms and signs may be taken as indicative of disease of the auditory nervous mechanism.

1. Impairment or loss of the bone-conduction of sound. When, in a deaf person, the note of a tuning-fork is no longer heard when it is in contact with the bones of the skull but is still heard aerially, the positive Rinne response to labyrinthine deafness is obtained. If in a case of unilateral deafness the base of a vibrating tuning-fork be applied to the vertex in the middle line, the sound will be heard better towards the deaf ear, if this is due to the conducting apparatus, and better, or altogether, in the sound ear if due to labyrinthine affection (Weber). If a vibrating tuning-fork be held upon the root of the nose or on the vertex, and the patient told to indicate when he ceases to *hear* the sound, the examiner is able to compare the length of time before he ceases to *feel* the vibrations. In labyrinthine diseases the patient ceases



to hear the sound from half a second to several seconds before the examiner ceases to feel them (Gardiner-Brown). At or after sixty years of age senile changes occur which render bone-conduction defective.

2. Impairment or loss of perception of notes of a high pitch; the voice, for example, being heard better than a watch. Galton's whistle is of value in testing such impairment. (For a description of the methods of testing the hearing power and the static sense, see Vol. IV. Part II. p. 351 *et seq.*)

3. The existence of vertigo and vomiting.

4. The presence of associated symptoms indicating disease of adjoining nervous structures. There is, as yet, no objective method by which deafness arising from disease of the auditory nerve may be distinguished from that due to lesion of the cerebral conducting tracts or centres, except by the presence of the associated symptoms referred to later.

Of certain phenomena, which may be taken as suggestive of labyrinthine disease, but which are in no wise conclusive, the following may be stated: audition is worse in a noise, whereas in middle-ear disease hearing is usually better in such circumstances (*paracusis Willisii*). There may be also a perversion of pitch, and a sensation of jarring produced by certain sounds. In such cases, also, inflation of the middle ear by a Politzer's bag not only fails to improve the hearing power, but frequently makes it temporarily worse.

**Varieties of Auditory Anaesthesia.**—(i.) Cortical and subcortical deafness. Cases of this nature due to tumour or softening involving the temporal lobe, and more especially the first temporal gyrus, are rare. The absence of any marked degree of deafness in cortical lesions is due to the extensive bilateral distribution of the auditory fibres in the cerebral cortex. A case has been recorded by Wernicke and Friedländer, in which complete deafness resulted from bilateral softening of the first temporal gyrus, whilst the examination of the ears both before and after death shewed an entire absence of any local changes; a case presenting somewhat similar features has also been reported by Mills.

The symptom more commonly met with as a result of unilateral destruction of the first temporal gyrus, and chiefly that on the left side in right-handed persons, is *word-deafness*, which may or may not be accompanied by some degree of deafness to ordinary auditory impressions.

(ii.) Deafness is only rarely found as a symptom of destructive lesions of the mid-brain, or of the pons Varolii.

(iii.) Deafness, unilateral or bilateral, is not uncommonly due to gummatous or other morbid states of the dura mater of the base, to inflammatory conditions extending from the bones of the skull, meningitis, or aneurysm. Unilateral deafness associated with cerebellar symptoms is indicative of a tumour in the cerebello-pontine angle. Many of these tumours, which are fibro-sarcomatous in character, grow from the sheath of the auditory nerve.

(iv.) The commonest causes of nerve-deafness are affections of the nerve terminations within the labyrinth. These conditions come properly

into the sphere of the aural surgeon. They are either primary disease of the labyrinth, to which the term Menière's disease is applied; or secondary to old-standing disease of the middle ear. (Vol. IV. Part II. p. 526.) Primary atrophy of the auditory nerve may occur in *tubes dorsalis*. Nerve-deafness may also be found as a stigma of hysteria, usually in association with and upon the same side as a hemianaesthesia.

Less can be said regarding the treatment of nerve-deafness than of any other form of cranial nerve palsy. For the various methods of treatment which have from time to time been recommended and adopted the reader is referred to articles in Vol. IV. Part II., and to special works on the subject. In other respects general principles should be applied in the treatment of deafness arising from intracranial disease.

**THE HYPOGLOSSAL NERVE.—The Hypoglossal Nucleus.**—The *chief hypoglossal nucleus* consists of a column of cells lying ventral to the central canal as long as this remains closed; but when this has opened out into the fourth ventricle, the nucleus forms the mesial part of the mass of grey matter forming its floor. The cells of the nucleus are roughly divided into three groups—internal, external, and posterior (Bruce). Within and around the nucleus are many medullated nerve-fibres. Some of these are the terminations of the pyramidal fibres, the *fibræ propriae* of Koeh; others belong to the “dorsal” and “posterior” longitudinal bundles.

Two accessory nuclei have been described in connexion with the hypoglossal nerve—Roller's small-celled nucleus and the nucleus of Duval. They do not give origin to any hypoglossal root-fibres.

Atrophy of the cells of the nucleus, which occurs in bulbar paralysis, is associated with atrophy of the root-fibres in direct proportion to the amount of cell-degeneration. The root-fibres spring from the nucleus of the corresponding side.

**Paralysis of the Tongue—Glossoplegia.**—Palsy of the tongue may occur upon one or both sides; in unilateral palsy defect is not apparent as long as the tongue lies still on the floor of the mouth; but on protrusion it is seen that the tip deviates towards the paralysed side, from the unopposed action of the unaffected genio-hyo-glossus muscle; a patient with this affection may also have difficulty in moving the tongue within the mouth towards the paralysed side.

In complete bilateral palsy the tongue cannot be protruded at all, it lies motionless on the floor of the mouth. Owing entirely to the mechanical difficulty thus produced, both articulation and swallowing are impaired. Should wasting of the muscular tissue of the tongue be present, in addition to paralysis, as occurs in nuclear and infra-nuclear affections, the mucous membrane is thrown into a number of prominent folds.

Paralysis of the tongue rarely occurs alone, being usually associated with a like affection of the lips, if from nuclear disease; with the soft palate

and the vocal cords, if from disease of the nerve-roots. If met with as an isolated symptom it is unilateral, and accompanied by wasting, from lesion of the nerve itself in the neck or floor of the mouth.

(i.) *Supra-nuclear Paralysis*.—It is rare for a cortical or subcortical lesion to be so limited as to involve the centre or the fibres proceeding from this without injuring the adjacent centres or tracts. Much more commonly a lesion in this region gives rise to palsy of the opposite side of the tongue with implication of the lower facial region; or the palsy of the tongue may merely form an item of a hemiplegia.

In the so-called pseudo-bulbar paralysis bilateral hypoglossal palsy is observed, but not alone, being invariably associated with weakness of the facial muscles, and sometimes with weakness of the limbs. This condition is distinguished from the bilateral lingual palsy of nuclear disease by the absence of wasting and by the retention of the faradic excitability of the lingual muscles.

(ii.) *Nuclear Paralysis*.—Atrophic degeneration of the cells of the hypoglossal nucleus is the earliest, and usually the chief pathological condition in bulbar palsy. It is also met with in tabes and syringomyelia.

Nuclear palsy is characterised by bilateral and usually symmetrical atrophy of the tongue, with inability to protrude it. Fibrillar tremors are not uncommonly observed, and the faradic excitability is sometimes diminished, though rarely lost.

(iii.) *Infra-nuclear Paralysis*.—There are three situations where the hypoglossal nerve, in common with the other cranial nerves, may be implicated between the nucleus and the periphery.

First, where the roots pass from the nucleus in the floor of the fourth ventricle to the surface of the medulla. A lesion in this situation, involving the hypoglossal nerve-roots and the pyramid on one side, produces a rare form of alternate hemiplegia, the tongue being paralysed on one side and the limbs on the opposite side.

Secondly, where the roots lie in the subdural space prior to their exit through the anterior condyloid foramen. In this situation the hypoglossal root-fibres lie in close proximity to those of the vagoglossopharyngeal nerve, so that the one set is rarely involved without the other; and the symptoms of a lesion in this situation are characteristic; namely, unilateral paralysis of the tongue and of the soft palate and of the vocal cord on the same side. Disease in this situation may be tuberculous, cario-necrotic, malignant, or syphilitic in nature, involving the meninges of the posterior fossa.

Thirdly, in the course of the nerve during or after its exit from the skull. The nerve-trunk is not uncommonly thus engaged in disease of the occipito-atloid articulation; merely, however, from its close proximity to this joint and its ready invasion by inflammatory exudations connected therewith. Hemiatrophy of the tongue may indeed be the only localising symptom of suboccipital caries.

It has been injured by wounds inflicted high up in the neck; and it has been implicated along with the sympathetic, the spinal accessory,



the vagus, and sometimes the glossopharyngeal nerves in tumours or glandular enlargements behind the angle of the lower jaw.

Hemiatrophy of the tongue has also been observed occasionally in association with facial hemiatrophy (*vide* "Facial Hemiatrophy," p. 167).

The treatment of hypoglossal paralysis is to be conducted according to the same general principles, and upon the same lines as described for the other cranial nerves. Electricity may be applied to this organ with advantage in cases of hemiatrophy, as well as in complete paralysis. The occasional association between lingual hemiatrophy and suboccipital caries should not be forgotten.

**THE VAGO-GLOSSOPHARYNGEAL NERVE.**—Considerable confusion has existed both in the nomenclature and in the descriptions of the mutual relations of the bulbar nerves—glossopharyngeal, vagus, and accessorius. Except outside the skull, where their distribution is clear, no means exist of distinguishing, anatomically, one from the other, either as regards their root-fibres or nuclei of origin, except inferentially by their position; the glossopharyngeal nerve being regarded as the uppermost, the accessory as the lowest of the series.

Before considering the results of recent investigation into this subject, let us inquire whether the nomenclature, as used in the textbooks, is quite correct. As Mr. W. G. Spencer has pointed out, the description of the roots of the bulbar nerves, as given by Willis, has not been universally followed. The term "accessory" was applied by this anatomist to the special nerve which is accessory to the vagi or "wandering pair," and which passes to the sterno-mastoid and trapezius muscles. Owing to a misuse of the term "accessory," it came to be applied to the lowest fibres arising from the bulb, which fibres do not belong to the accessory nerve, but to the vagus, as Willis indeed had shewn. Hence the nerves of bulbar origin are, in addition to the hypoglossal, the glossopharyngeal and vagus; whilst the accessory nerve, or nerve of Willis, is of purely spinal origin. In the accompanying detailed account of the nuclei of origin of the bulbar nerves, it is shewn that the glossopharyngeal and vagus are really parts of one great mixed nerve; that they have a common nucleus of origin of their efferent (motor) fibres; and that their afferent fibres terminate in the so-called posterior end-nucleus, and in the "ascending" glossopharyngeal root or "fasciculus solitarius" and its related end-nucleus.

**The Vago-glossopharyngeal Nuclei.**—These nuclei consist of two parts; a motor nucleus, or nucleus ambiguus, and a sensory nucleus, or posterior vago-glossopharyngeal nucleus.

(a) *Nucleus Ambiguus.*—This nucleus extends from the level of the fillet decussation, proximally, as far as the exit of the upper glossopharyngeal root-fibres. It is, therefore, coextensive with the posterior division of the nucleus, but occupies an antero-lateral position in the medulla. It is recognised by the position of its cells, which lie *upon* and *mesial* to the vago-glossopharyngeal root-fibres. The *efferent* fibres pass



directly outwards from the nucleus as the lowest roots of the vagus nerve ; whilst in the upper portion they assume a dorso-internal direction before bending outwards as the upper fibres of the vagus and glossopharyngeal nerves.

The *nucleus ambiguus* is the nucleus of origin of the motor fibres for some of the muscles which move the vocal cords, and probably also for the levator palati muscle. In many cases of bulbar paralysis the cells of this nucleus have been found to be atrophied.

(b) The *posterior vago-glossopharyngeal nucleus* is the end-nucleus of those afferent fibres of the vago-glossopharyngeal nerve, which arise in the jugular and petrosal ganglia and the ganglia of the vagus.

(c) *The Fasciculus Solitarius, or "ascending" Glossopharyngeal Root.*—A third factor is to be studied in connexion with the vago-glossopharyngeal root-fibres. The *fasciculus solitarius* derives its fibres from both the ninth and tenth nerves and probably also from the nerve of Wrisberg. This bundle is traced as far as the lower end of the medulla oblongata.

Division of the glossopharyngeal nerve-roots is followed by degeneration of many of the intra-medullary root-fibres ; these may be traced both into the *fasciculus solitarius* and, to a less extent, into the posterior glossopharyngeal nucleus.

From these observations it is seen that the spinal glossopharyngeal root is analogous with the spinal trigeminal root, both of which are composed of afferent fibres, passing to their end-nuclei, and springing from the cells of ganglia which are situated on the nerves outside the brain.

The vago-glossopharyngeal nerve is therefore both motor and sensory in function. The peripheral distribution of the nerve, which it is scarcely necessary to follow in detail here, as it may be studied in any anatomical textbook, is most extensive ; structures so far differing in position and in function as the soft palate, the vocal cords, the pharynx and oesophagus, the lungs, the heart, the stomach, and to some extent the intestines, receive a portion of their nerve-supply through this nerve.

TABLE shewing the Functions of the Vago-glossopharyngeal Roots,  
modified from W. G. Spencer

	<i>Afferent.</i>	<i>Efferent.</i>
Upper roots : 9th or glossopharyngeal nerve	{ Respiratory regulating fibres { Respiratory exciting fibres (inspiration) { Superior laryngeal Respiratory inhibitory fibres (expiration)	Cricothyroid (?) Stylopharyngeus Oesophagus Pharyngeal constrictors
Middle roots—10th or vagus nerve	{ { Bronchial	{ Gastric branches { Bronchial muscles { Inferior laryngeal { Cardio-inhibitory ; levator palati
Lower roots of vagus nerve	no afferent fibres	{ Sterno-mastoid { Trapezius (upper part)
Spinal accessory nerve (of Willis)	no afferent fibres	

It is not to be supposed that there is a hard and fast line between

the upper and middle roots, or between the middle and lower, as might be implied by this table; the general statement may be made that experiment has shewn that the upper vagal roots are more concerned in inspiration than the middle, which chiefly subserve expiration. The fibres more especially related to inhibition of the heart lie in the lower root-bundles.

**Vago-glossopharyngeal Paralysis.**—A. *Paralysis of the glossopharyngeus.*—There is no case of localised unilateral paralysis of the glossopharyngeal root-fibres on record; so that the derangement of function produced by such a lesion has to be inferred by a process of exclusion from the connexions formed with other adjacent nerves, and from experimental data. It is stated that the trunk of the nerve contains the fibres subserving taste for the posterior third of the tongue, and it is probable that these fibres reach the brain by the glossopharyngeal roots. (See p. 525.)

Nerve-fibres for the muscular apparatus of the oesophagus pass outwards in the uppermost of the vago-glossopharyngeal roots. Outside the skull these fibres enter the vagus, through which they are distributed by its recurrent laryngeal branch. But the pharyngeal plexus may play a part in this connexion, for it is probable that it receives its motor fibres directly from the vagus, through the pharyngeal branch. As the stylopharyngeus muscle receives a branch from the glossopharyngeal nerve it is inferred that it receives its motor supply from this source. But whether these fibres are contained in the glossopharyngeal root, or are derived from the facial, is unknown. Symptoms of glossopharyngeal palsy are difficulty in swallowing, anaesthesia of the upper pharynx, and loss of taste over the posterior third of the tongue.

B. *Laryngeal Paralysis.*—This is the most important feature in vago-glossopharyngeal palsy. As is well known, the larynx is supplied by two branches of the vagus; the superior laryngeal, which is the sensory nerve of the mucous membrane in the upper portions of the larynx, is motor for the cricothyroid muscle and the epiglottideus; and the recurrent laryngeal supplying the remaining muscles and the mucous membrane of the part below the vocal cords and the trachea.

The kinds of laryngeal palsy, partial or complete, have been described (Vol. IV. Part II. p. 259 *et seq.*), but a short summary of their symptoms may be stated:—

(a) Total bilateral palsy. Aphonia, no cough, and stridor only in deep inspiration. Both vocal cords motionless and in the cadaveric position. Due to organic causes only.

(β) Total unilateral palsy. Voice hoarse, no cough, stridor usually absent, but may be present on deep inspiration. The paralysed cord is motionless in the cadaveric position. Due to organic causes.

(γ) Bilateral abductor palsy. Voice normal, cough normal, inspiration difficult and accompanied by a loud stridor. Cords approach on phonation, but do not separate on inspiration. Usually organic, but appears to be occasionally of functional nature.

(δ) Unilateral abductor palsy. Voice and cough scarcely affected. Paralysed cord immobile during inspiration. Both cords approach on phonation. Usually organic.

(ε) Adductor palsy (always bilateral). Aphonia, no cough or stridor. Cords normal during inspiration; no movement on attempt at phonation. Usually functional.

**Varieties of Laryngeal Paralysis.**—(i.) *Cortical and Subcortical Laryngeal Palsy.*—A number of cases have been recorded in which palsy of the vocal cords is said to have resulted from cortical and subcortical lesions. The general statement may be made that, so far as clinico-pathological observation has yet shewn, there is no clear evidence that a unilateral cortical lesion is followed by palsy of the vocal cords on one or both sides.

(ii.) *Nuclear Paralysis.*—In chronic nuclear degeneration the muscles of the larynx are rarely paralysed alone; there is an associated paralysis of the muscles of the soft palate and usually also of the pharynx. When in association with such symptoms there exists palsy of the lips and tongue, the condition known as chronic progressive bulbar paralysis is obtained. Nuclear paralysis of the degenerative type is usually bilateral.

The extent of the laryngeal palsy in all such cases is due to the amount of degeneration of the nucleus ambiguus, for it is rare even in advanced cases of bulbar palsy to find this nucleus completely atrophied. The great longitudinal extent of the nucleus and its close connexion with the functions both of phonation and deglutition, as suggested by Sir W. Gowers, probably account for much of the variation which has been observed.

Associated with the palsy of nuclear degeneration is usually to be found a diminution or loss of reflex action from the soft palate, pharynx, and larynx; but common sensibility is retained.

In bulbar paralysis there is an associated degeneration of the cells of the anterior horns of the spinal cord, with wasting of the limb muscles. Laryngeal palsy may also be a phenomenon of tabes dorsalis, general paralysis of the insane, and syringomyelia.

(iii.) *Peripheral Laryngeal Paralysis.*—The course of the trunk of the vagus and its recurrent laryngeal branch is so extensive that it may be involved by disease, usually from compression, both in the neck and the upper part of the chest. Experimental section of the vagus trunk is followed by complete palsy of the vocal cord upon the side of lesion; but should the section be performed above the point of emergence of the superior laryngeal branch, anaesthesia above the level of the paralysed cord is also obtained.

It is, however, rare for a tumour or other growth, at all events in the early stages, to destroy the continuity of all the nerve-fibres so effectually as to produce this result. The symptom most commonly obtained is paralysis of the abductor mechanism only.

*C. Paralysis of the Soft Palate.*—All experimental and clinical evidence is in favour of the bulbar innervation of the levator palati muscle.



From the trunk of the nerve the palatal fibres find their way into the pharyngeal plexus, and thence to the levator musele, while the laryngeal nerve-fibres continue in the vagus trunk.

Paralysis of the soft palate, whether unilateral or bilateral, is only recognised when the patient is made to phonate. In complete bilateral palsy there is no palatal movement on saying the vowel "ah," and the pronunciation of those words requiring closure of the naso-pharynx is rendered imperfect; hence "rub" is pronounced "rum," and "egg" as "eng." Bilateral palsy may exist in all degrees, from the complete form best seen as an early post-diphtheritic phenomenon to the incomplete variety in bulbar palsy. In unilateral paralysis there is said to be, when at rest, a lowered and less arched condition of the velum pendulum palati, but this sign, if it exists, is not to be relied upon. The only true evidence of palsy of one side of the palate is the absence of movement of that side on phonation, the opposite side being freely elevated. The position of the uvula is of no clinical value in this relation.

In the treatment of vago-glossopharyngeal palsy the same principles should be borne in mind as in like affections of the other cranial nerves. Owing to the extensive distribution of the nerve and the long course of its trunk in the neck and chest, it is much more liable to implication by disease of an extra-cranial nature than any of the other cerebral nerves.

The degenerative diseases do not permit of any satisfactory form of treatment, but the most favourable methods are given under bulbar paralysis (p. 724). For the treatment of local laryngeal affections the reader is referred to special textbooks and to Vol. IV. Part II. p. 275.

**THE SPINAL ACCESSORY NERVE.**—The eleventh nerve of Willis, or spinal accessory nerve as it should be called, arises from a group of cells situated on the dorso-lateral aspect of the anterior horn of the spinal cord, over an area corresponding to the origin of the first five cervical nerve-roots. The cells of both these sets of nerve-roots lie in the anterior horn; but the root-fibres of the spinal accessory pass dorso-laterally through the lateral column of the spinal cord to make their exit ventral to the posterior horn, whilst those of the cervical nerves pass antero-laterally to form the anterior nerve-roots.

Formed by the union of nerve-roots arising in the manner just described, the spinal accessory nerve takes an upward course, and passes into the cranium through the foramen magnum. Here it approaches the vago-glossopharyngeal nerve, and issues with it through the jugular foramen. In this situation also it lies in close proximity to the root of the hypoglossal nerve.

It supplies two museles, the sterno-mastoid and the upper part of the trapezius.

**Paralysis of the Spinal Accessory Nerve.**—As just shewn, this nerve has a spinal origin, and a cranio-spinal course; and it passes out of the cranial cavity in company with, and in close relation to, purely cranial



nerves. Hence we find that it may be implicated in disease of the spinal cord and subdural space, in the upper part of the vertebral canal or in the posterior fossa of the skull. The sterno-mastoid and trapezius muscles may therefore be paralysed as a result of chronic degenerative atrophy of the cells of the anterior horns, as occurs in progressive muscular atrophy, in *tabes dorsalis*, and *syringomyelia*. On the other hand, they may be paralysed in company with the soft palate, pharynx, vocal cords, and tongue, as a result of disease implicating the nerve-roots of the posterior fossa. They may also be paralysed from disease of the membranes or bones in the occipito-atloid region, or from injuries inflicted in this neighbourhood. The nerve may be affected alone outside the skull either from injury or from the pressure of new growths, or by implication in inflammatory conditions situated deeply in the upper part of the neck.

The **symptoms** of lesion of this nerve are paralysis of the sterno-mastoid and trapezius muscles. Paralysis of the sterno-mastoid muscle impairs the rotary movement of the head to the opposite side. This movement is not entirely lost, owing to the unimpaired action of the deeper neck muscles, which are also rotators of the head at the atlo-axial joint. The paralysis is associated with wasting and consequent loss of the prominence which the normal muscle occasions at the side of the neck.

Of the three divisions into which Duchenne divided the trapezius, the upper two, and chiefly the uppermost, are affected. The rounded contour of the neck and upper part of the shoulder is lost from the atrophy which accompanies the paralysis. In bilateral paralysis the movement of shrugging the shoulders in which this muscle takes a part is impaired, and the chin tends to fall forwards on to the sternum.

The **treatment** of paralysis of the spinal accessory nerve is that of the morbid condition, general or local, causing the paralysis; and the nutrition of the muscles should be maintained by the application of faradism, or galvanism, according to the electrical reaction.

**MULTIPLE PARALYSES OF THE CRANIAL NERVES.**—Under this heading it is intended to give a short description of the paralyses of the cranial nerves which occur commonly in groups of two or more; especially with reference to disease of the nerve-roots as they pass through the subdural space and basal membranes to find exit by the foramina at the base of the skull.

A superficial examination of the base of the skull shews that it is readily subdivided into three divisions: the anterior, middle, and posterior fossae respectively; and an inspection of the mode of exit of the cranial nerve-roots indicates that each fossa has a group or groups of nerve-roots passing from it.

Thus the anterior fossa, formed by the orbital plate of the frontal and the cribriform plate of the ethmoid bones, contains the olfactory bulbs and tracts, and, quite at its posterior extremity, the optic nerves and chiasma; the fossa itself containing the frontal lobe.

In the middle fossa, which contains the temporo-sphenoidal lobe, lie two groups of nerves : in the anterior part the oculomotor nerves (3rd, 4th, and 6th), with the ophthalmic branch of the fifth ; and, posteriorly, the Gasserian ganglion with its three divisions ; whilst the optic chiasma occupies an important mesial position.

In the posterior fossa are situated the cerebellum, the crura cerebri, pons, and medulla oblongata ; and from the side of the latter structures issue several groups of nerves. Quite at the anterior margin of this fossa, mesially, is the origin of the third cranial pair. Immediately behind, but lying laterally, are the motor and sensory roots of the trigeminus. The motor root arising higher up and somewhat dorsally to the sensory, turns round the latter so to lie in the middle fossa ventral to the Gasserian ganglion. Passing posteriorly and mesially, the sixth pair are seen to pierce the dura mater to enter the middle fossa. Lying immediately outside this pair are the facial and auditory nerves, hidden from view when exposed from above by the flocculus cerebelli and its peduncle. Of these two nerves the auditory is the more dorsal, and they both leave the fossa by the internal auditory meatus. Immediately behind them, and in the same line, lies the vago-glossopharyngeal and accessory group ; and parallel with this set, but more mesial, is the series of hypoglossal root-bundles.

The cranial nerves may be paralysed in groups by disease in the several fossae ; and a study of the combinations thus induced may lead to an exact diagnosis of the site of the lesion.

Unilateral loss of the sense of *smell* from disease of the anterior fossa is rarely met with ; but if it occurs with other symptoms pointing to a tumour of the frontal lobes, its presence is of great localising value.

The symptoms of lesion of the *optic chiasma* and tracts have been already referred to in detail (p. 503), so that it is only necessary here to accentuate the fact that lesion of the optic chiasma, the common cause of which is tumour or enlargement of the pituitary body, is characterised by the phenomena of bitemporal hemianopsia.

But the *middle fossa* is not uncommonly the seat of inflammatory or other conditions of the dura mater involving the cranial nerves. Paralysis of the oculomotor nerves together with the ophthalmic branch of the trigeminus is the combination of nerve palsies characteristic of disease of the anterior part of the middle fossa, chiefly about the cavernous sinus ; and in inflammatory states and new growths protrusion of the eyeball has been observed.

A unilateral lesion of the sensory trigeminal nerve, complete or partial, with or without affection of its motor root, is characteristic of a lesion of the posterior part of the middle fossa, in the neighbourhood of the Gasserian ganglion. This is often the earliest sign of a tumour of the base of the skull.

Coming now to the *posterior fossa*, the auditory and facial nerves are usually paralysed together, either on one or both sides, the former, when

occurring with cerebellar symptoms, being characteristic of a tumour of the cerebello-pontine angle.

Motor and sensory trigeminal palsies are associated in basal affections of the anterior part of this fossa, involving the roots of the fifth nerve.

The vago-glossopharyngeal, accessory, and hypoglossal group are usually paralysed together; seeing that they arise, pass through the subdural space, and eventually issue from the skull, in close proximity to each other.

In respect of the causation of these conditions the several processes of disease which occur at the base of the skull have to be considered. Of these by far the commonest is syphilis. From this cause a gummatous basal meningitis arises which grips, and eventually compresses, the nerve-roots as they pass through the subdural space.

Next in frequency come new growths of the bones of the base of the skull, and tumours of the nerve-sheaths, more especially the auditory nerve, and of the membranes.

Tuberculous disease of the bones and membranes is less frequently found. The nerves may also be torn or injured in fractures of the base of the skull.

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For reference to the subject as a whole the reader should consult standard text-books in Neurology, both in the English and German languages.

W. A. T.

## TRIGEMINAL NEURALGIA

By HENRY HEAD, M.D., F.R.S.

**Introduction.**—The word neuralgia, strictly used, signifies a pain which follows the course of some peripheral nerve or nerve-root, but is not caused by any gross organic lesion of any part of the nervous system. However, such a use of the word is impossible in practice, for it involves the introduction of pathological qualifications.

Vulgarly, neuralgia is used to signify any pain which appears to shoot along the course of a nerve. But since a large number of such pains are caused by definite well-known organic diseases of the nervous system, the name neuralgia has been clinically used to denote any pain of this character which cannot be attributed to some one of these. For, if the character of the pain only were relied upon, it would be impossible to separate the lightning pains of tabes, or the pain which follows herpes ophthalmicus, from true neuralgia; yet both are now known to be due to organic disease. Again, the discovery of neuritis at once removed brachial and sciatic neuralgia to a position amongst the symptoms of this newly formed disease-group. Thus, the more our knowledge of organic and functional disease of the nervous system advances, the smaller becomes the group of pure neuralgias.

Again, the group of pure neuralgias has been much diminished of late by observations in another direction. It was well known before Valleix's time that a pain clinically resembling neuralgia might be produced not only by disease of the nervous system, but also by disease of some internal organ. Valleix is careful to explain that in none of his cases of neuralgia was visceral disease present—a statement that an examination of his records, in the light of our present knowledge, by no means bears out. Thus an increased knowledge of the referred pains of visceral disease has further reduced the group of idiopathic neuralgias, by referring such pain to the position of a symptom of visceral disease.

Progress in both directions has been so great of late years, that we are almost justified in believing that most neuralgias will ultimately be classified as symptoms of disease in some part of the nervous system (either peripheral or central), or as the expression of the reaction of the nervous system to visceral irritation. Thus neuralgia is in most cases not a disease, but a symptom; and the greater part of the contents of this section are and should be broken up and distributed about this *System of Medicine*. As, however, the word is in popular use, and the determination of the true focus or cause of the neuralgic pain is often extremely difficult, an attempt will be made to treat of the various



affections still known as neuralgia, and to shew how far we are able to assign them to their proper places.

As many different conditions are included under the name neuralgia, they will be considered in the following order:—

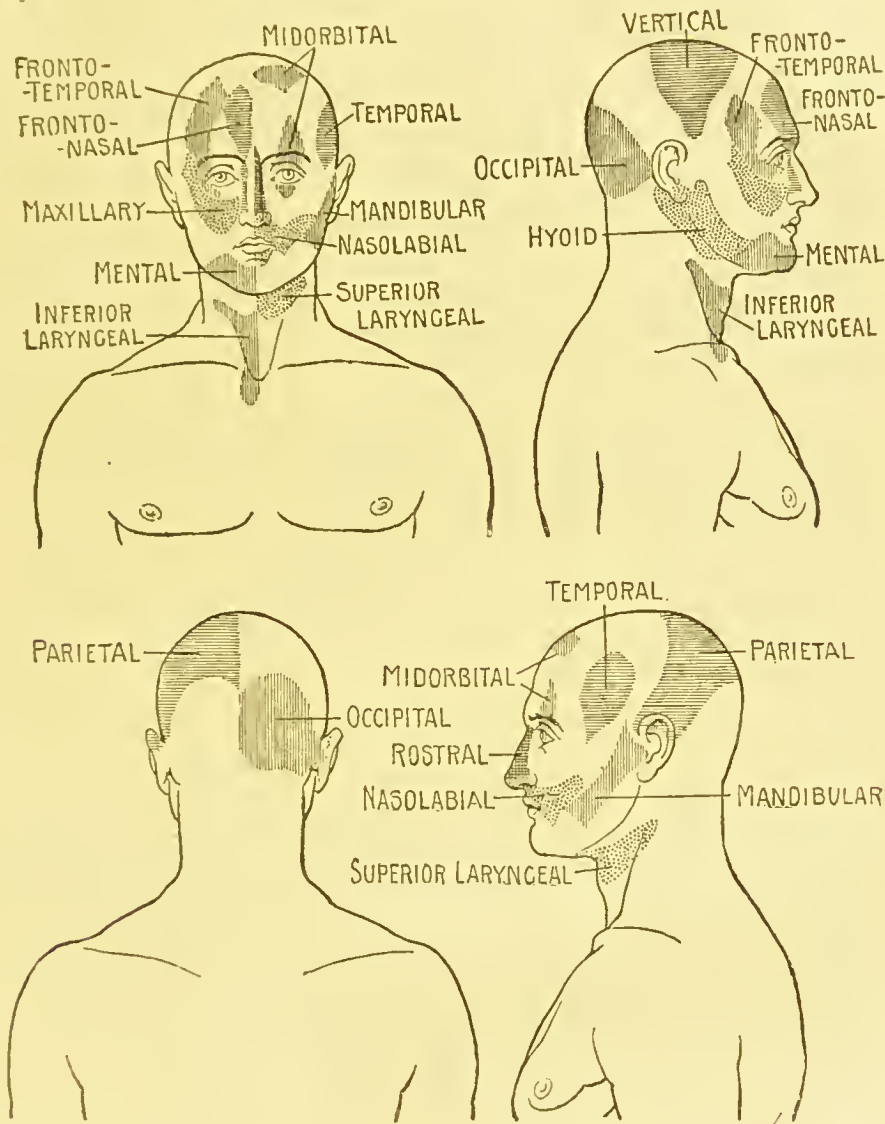


FIG. 75.—The "segmental" areas of the head and face.

(1) Neuralgia quinti major (tic douloureux, epileptiform neuralgia). I propose to shew that this is a definite disease of the nervous system, with a distinct course and character.

(2) Neuralgia secondary to disease of the nerves of the head; for example, tumours involving the fifth nerve, post-herpetic neuralgia, and

the like. These conditions are often extremely difficult to discriminate during life from neuralgia major or minor. Such pains as are part of multiple neuritis will be considered elsewhere.

(3) Neuralgia minor. This group contains:—(a) True referred visceral pains due to disease of the intimate structure of some organ of the head; (b) Pains due to disease of the membranes or tissues surrounding some organ, or to actual affection of the finer nerve-twigs by the morbid process; (c) Neuralgias of the head and face arising as direct consequences of disease in organs other than those of the head.

(4) Neuralgias arising from general bodily states, such as neurasthenia, psychasthenia, and hysteria.

#### Central and Peripheral Nervous Supply to the Head and Neck.—

(1) *Distribution of the Trigeminal.*—The peripheral distribution of the branches of the fifth nerve can be mapped out by three methods:—

(a) By dissecting each branch to its finest termination. This is extremely laborious, and must always fail to shew the complete supply

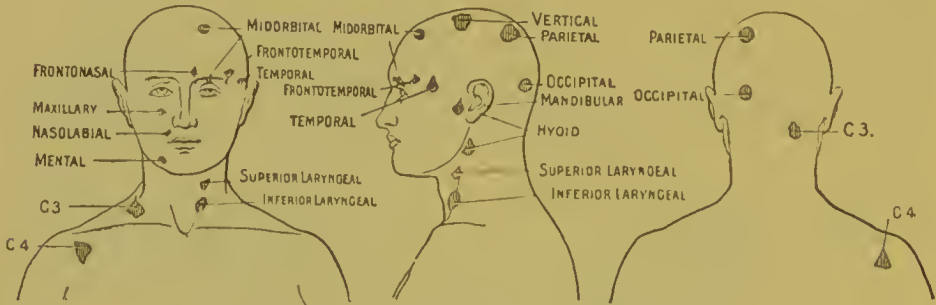


FIG. 76.—The “maxima” of the segmental areas shewn in Fig. 75.

of the nerve, owing to the difficulty in determining the limits of supply for the finest branches.

(β) By observing the anaesthesia produced by division of one or more branches. This method shews only the area on the skin supplied solely by the nerve divided, and the result will therefore fall short of its full supply.

(γ) On the other hand, we can avail ourselves of an ingenious method, invented by Prof. Sherrington, for mapping out the posterior roots upon the body. This method, which may be called that of “residual aesthesia,” can best be elucidated by an example. Supposing the first and second divisions of the fifth nerve to have been divided, the border of the anaesthesia so produced will represent the extreme anterior limit of the supply of the third division of the fifth, excepting where it meets the cervical nerves of the vertex. In the same way, if all three branches of the fifth have been divided, the limit of the anaesthesia will represent the anterior border of the posterior root of the second cervical.

(2) “*Segmental*” *Areas of the Head and Neck.*—When an organ, such as the eye or one of the teeth, is affected, pain is not situated only in the

organ itself, but is referred to parts at a distance on the scalp or face. Such referred visceral pains, when of sufficient severity and duration, are accompanied by areas of superficial tenderness. These areas represent the segmental origin of the nerves for pain to the head; they do not represent the distribution of the peripheral branches of the cranial nerves. Fig. 75 is given to shew their character and distribution, in order to facilitate reference in later parts of this article. When the tenderness is not very severe these areas may be present in part only. Certain spots in each area are then found to become tender sooner, and to remain tender longer, than any other parts of the area. These maxima are of practical importance, because they are the spots to which the patient refers his pain, whether the pain be accompanied by superficial tenderness or not (Fig. 76).

**Neuralgia quinti major.**—*Tic douloureux, epileptiform neuralgia.*—This form of neuralgia has been placed in a group apart, owing to the marked similarity that one case bears to another, both in course and symptoms. In the earliest stages each case appears to be one of simple neuralgia, and under this impression relief has been sought in removal of teeth or other operative procedures. At last the full clinical picture of this hideous disease unrolls, varying only in unessential details from the classical type.

The story of most of these cases is somewhat as follows:—A man or woman, between thirty-five and sixty years of age, apparently in fair health, is suddenly attacked with pain within the peripheral course of one of the branches of the trigeminal. The pain is continuous for some hours or days. The teeth are attended to without relief; or perhaps the removal of a tooth, apparently sound, is coincident with the cessation of pain, and the patient imagines he is cured. But after a varying interval the pain recurs, and at last no day passes without an attack of greater or less duration. Throughout this time the patient is able to continue his work without much interruption; but gradually the attacks increase in severity and frequency till all consecutive work becomes impossible. The onset of the first attack is usually, as far as the patient can tell, without obvious cause. Later attacks may seem to be due to some change in the weather; and for this ill-defined influence of weather there is an analogue in the lightning pains of tabes. Abnormal physical states of the body, such as constipation, and more particularly such mental conditions as a sudden shock, anxiety, business worry, and the like, are peculiarly apt to induce an attack in this stage of the disease. At first the attacks of pain may be limited to the territory of one branch of the nerve, to that of the inferior dental branch of the third division, for instance. But, sooner or later, the pain spreads to other branches on the same side of the face, until at last all three divisions may be more or less affected. The attacks also alter in frequency. Throughout the space of many hours daily the patient is racked by paroxysms of pain at regular intervals, enduring from a few seconds to many minutes. Sleep, except

under anodynes, becomes impossible; the patient dare not eat, talk, or smile, for fear of precipitating a paroxysm. Life thus becomes utterly unbearable, and is sometimes ended by suicide.

In the simplest cases the pain affects one spot in the jaw or face; but generally more than one spot is affected, and from these points the pain radiates along the course of some nerve branch. In a case in which the pain was situated at a single spot in the upper jaw, it was said to resemble "the sudden thrust of a red-hot gimlet into the flesh." More commonly the pain starts at one spot, and rapidly radiates along the course of the nerve. It cannot be said to shoot from one point to another, but, starting at one focus, the pain radiates along the course of the nerve "as if a red-hot electric wire was plunged into the face and the current affected the whole nerve." If two spots form radiating foci the pain in any paroxysm may start from them simultaneously or successively, but does not definitely dart from one to another. Uncommonly, radiation may take place into the occipital region or into the neck; although, since the pain in this region is removed by ablation of the Gasserian ganglion, there is no reason to suppose the territory of these nerves to be primarily affected.

The pain never starts at a spot outside the territory of the fifth nerve, though radiation may take place beyond its boundaries. It is rarely bilateral; Krause describes one such case, and I have seen this bilateral distribution in an old woman of seventy-five, in whom the disease had lasted twenty-five years.

The spots from which the pain radiates are always described as situated below the skin. Thus, a not uncommon distribution is for the pain to start from a spot exactly above the highest point of the curve of the ala nasi, and thence to dart around the eye on the inner and the outer side, until a patch is affected on the forehead about the size of the palm of the hand, extending from the upper lid to the root of the hair. Here the pain is throughout "just under the skin." Another common starting-point is just posterior to the canine of the lower jaw. Here the stab of pain begins, and rapidly radiates along the whole lower jaw. It may then stop, but sooner or later it will pass from a deep course in the lower jaw to radiate over the posterior part of the temporal fossa. Not uncommonly a second painful focus is perceived over the posterior part of the zygoma. Another extremely common spot is exactly over the infra-orbital foramen, and from this point the pain radiates over the cheek and anterior part of the temporal fossa. Sometimes the lateral border of the tongue is the seat of a focus of pain, from which radiation takes place over the same half of the tongue excepting only the posterior part of the dorsum. Thus the pain tends to start at certain points which mostly correspond to the exit of nerve-bundles from the deep structures of the face, or to their terminations upon the surface. From such foci radiation takes place mainly along the distribution of the affected nerve branch. But the matter is not quite so simple as it seems at first sight. For although the pain may



start at the angle of the nose, and affect the eye and forehead, complete extirpation of the first division of the fifth may still leave the nasal point unaffected. Moreover, after such an operation the anaesthesia of the scalp extends back to the parietal eminence, and is of wider extent than the previous pain.

Krause states, and in this respect my experience absolutely bears out his statement, that pressure with the finger may start a paroxysm, or may simply increase that dull sense of pain which exists over the area of radiation between the paroxysms. Moreover, in such cases tender points can frequently be found over the exit of nerves other than those directly affected in the paroxysm. When it occurs at stated intervals, pressure or even the lightest touch in such a point will not uncommonly precipitate a paroxysm; whilst immediately after it has passed, pressure, whether heavy or light, is without obvious effect. Moreover, in the paroxysm itself most patients firmly press the hand or some hard object to the face, and apparently gain some ease by this action. Lastly, there are a certain number of cases of undoubted severity in which no tender point can be detected.

As I have said, the first attack starts without any obvious cause and when the patient is not conscious of any deviation from his general health. I have seen one case, however, in which the first attack began two weeks after a blow on the side of the head from the main boom of a yacht.

After the disease is once established the season of the year may determine an attack. In a case of Krause's the attacks came on in the spring, and only for a period of six weeks; for the rest of the year she remained free. One of my patients suffered from February to October for many years; but the period shifted, and he then suffered in the winter months only.

Any marked deterioration of physical health, such as may be due to a common nasal catarrh or constipation, will tend to bring on an attack.

Mental shock is a potent factor in inducing these attacks. One of my patients remained free from attacks for sixteen months after the inferior dental nerve had been stretched. But within an hour after seeing a fellow-workman killed by a fall the pain came on worse than ever it had been before. Business worry or family anxiety acts in a similar way, and even an access of anger may induce an attack.

During the period of an attack the actual paroxysms are affected by the most diverse conditions. A breath of wind, a slight touch on the beard or hair, talking, drinking, deglutition, or even swallowing the saliva, will precipitate a paroxysm or increase its severity. Thus the patient lets his hair and beard grow, the saliva may dribble from his mouth upon the pillow, the tongue and cheeks may become foul from decomposing food; yet he dare not utter his wants. The act of defecation is commonly attended by an increase in the severity of pain, and the patients therefore shun going to stool, and thus aid in the production of the constipation so commonly present. As a general rule during the attacks a

cold blast of air from an open window is unpleasant, and is said to increase the severity of the paroxysm. But atmospheric heat and cold cannot be said to have any definite effect in determining the attacks in a patient already suffering from the disease. The effects of hot and cold water in the mouth are extremely variable. In some cases, especially those in which the lower jaw and tongue are not affected, neither hot nor cold water has any effect on the paroxysms. Sometimes hot water seems to relieve the pain, sometimes it is unpleasant; in other cases cold water may be without effect, or sometimes it may increase the paroxysms. Thus each patient will regulate the temperature of his food according to his particular experience.

In the earlier stages of the disease the attacks last a shorter time; but each attack tends to be continuous, and is not made up of a chain of paroxysms separated from one another by longer or shorter periods of freedom from pain. In one of my cases the first sign of disease was an attack, of sudden onset, lasting continuously for over a week. Later he suffered from one short attack daily of about half an hour's duration; ultimately a paroxysm appeared every five minutes throughout the three days I had him under close observation. When periodicity is well established the paroxysms may return at almost any interval. The most frequent I have seen recurred with almost precise regularity every forty seconds for several days in succession; on the other hand, some patients have only one short daily paroxysm at exactly the same hour.

In the earlier stages the pain ceases if the patient can get to sleep, and does not return during the time he is asleep; but during the later stages the paroxysms continue with the same regularity day and night, for sleep becomes impossible.

The pain is accompanied by marked vascular, trophic, and secretory changes. A more or less permanent red flush suffuses the affected side, which may deepen with each paroxysm. The conjunctiva is reddened. The hair and beard change colour, or may fall out. Or again, either or both may be rubbed away by the pressure exerted by the patient on his face during the paroxysm. The affected cheek not uncommonly appears peculiarly greasy. The patient may complain that some part of his face, such as the lip, feels swollen, and he is convinced that it is larger than normal. A similar feeling of swelling also exists over those parts of the jaw which are tender. In one of my cases the two painful spots were marked out by trophic changes over an area of the skin about the size of a sixpence; the skin here appeared raised, thickened, and very dark in colour. These spots disappeared entirely when, after treatment, the pain left her, and she stated that they always came and went coincidentally with the pain.

During an attack, especially within the territory of the first and second divisions of the nerve, tears flow copiously, and intense photophobia may exist. With an attack over the third division saliva may be secreted. Occasionally a discharge of thin fluid takes place from one nostril, apart from lachrymation. A metallic taste may also be complained

of over the affected side of the tongue. Apart from the foulness of the mouth, the appetite is, as a rule, unimpaired, and the patients do not waste. Constipation is commonly present during the period of attack, owing in part to the dread of defecation.

The mental condition is at first merely that of a person suffering pain—irritable and depressed, but fairly cheerful in the inter-paroxysmal periods. Later, partly owing, no doubt, to the enormous doses of hypnotics and anodynes necessary to still the pain, the patient may become insane. The form assumed is that of an acutely suicidal melancholia. Krause states that even when of considerable duration this insanity is curable after the pain has been relieved by operation. But, apart from insanity, suicide is common, and every patient in the later stages of the disease should be looked upon as a possible suicide. Neither hallucinations nor delusions are common, but the memory becomes extremely bad for all recent events.

During each paroxysm the agony causes the patient's face to be drawn up. But, apart from this expression of emotion, the facial muscles seem in some cases to participate reflexly in the paroxysm. Each slight attack is then accompanied by a fibrillar tremor that can have nothing to do with expression.

*Etiology.*—In spite of all that has been written on the subject of the heredity of this neurosis, nothing can be clearer than that the subjects of neuralgia major are in no sense of the word neurotic; nor have they a neurotic heredity. To say that some ancestor suffered from "paralysis" no more constitutes a neurotic inheritance than a similar history of "dropsy" would necessarily indicate a tendency to renal disease. In the clinical records of cases of neuralgia major it is striking how few cases are hereditary neuropaths. Krause is particularly emphatic in the statement that the cases that came under his observation were in no way inheritors of nervous disease. Sir V. Horsley in his large experience has only found one case in which there was a history even of "paralysis." In ten consecutive cases I could find none in which there was a history of any nervous disease or insanity in the family. Again, the subjects of neuralgia quinti major, unlike so many of those who suffer from neuralgia minor, are not themselves neuropaths. With the exception of their one ailment, they are healthy persons. To say that a man, who has suffered from agonising pain every forty seconds day and night for a fortnight, is neurotic because he is disposed to be irritable or to cry, betrays a lack of imagination in the observer. Once relieve the pain by operation, and these patients will prove to be quiet, intelligent, and normal human beings. They may perhaps shew a tendency to early arterial degeneration; although, as most of them have already reached the age at which slight arterial degeneration might be expected, such observations are of but little value. The great age to which many of these patients live is in itself a testimony to their inherent soundness.

The disease seems to be about equally distributed between the two sexes. Among Sir V. Horsley's patients who came to operation there is



slight preponderance of women. Sir V. Horsley's youngest patient was twenty-one at the time of onset; his oldest fifty-eight; the ordinary age of onset lies between forty and fifty.

*Pathology.*—If we look back at the history of each case we find that the disease has invariably been mistaken for neuralgia minor at first, but has rapidly shewn that it belonged to the graver type. Very commonly it begins in the upper or lower jaw, in the region of one of the teeth, but never, as far as my experience goes, in the tooth itself. In all true cases of major neuralgia the pain is strictly confined to one-half of the face or head. It may start at one point in an edentulous jaw, or in the whole of one side of the jaw as far forwards as the point of insertion of the canine. The subsequent history is always the same. A dentist is applied to, who rightly clears the jaw from decayed stumps, and then proceeds to remove sound teeth. This gives the patient transitory relief, or no relief at all; the pain then rages as before in an edentulous jaw. The pain may also start about an eye that is absolutely healthy. Thus, unlike neuralgia minor, and especially unlike referred visceral pain, no obvious cause or connexion can be found between the onset of the pain and disease of any peripheral organ to which the nerve terminals are distributed.

Many observations have been made on portions of nerve extracted by surgical operation, but up to the present time without satisfactory results. Dana found no change in the nerve elements, but an endarteritis of the vessels of the nerve-sheath. Putnam found the same endarteritis, but also changes in the nerve elements and the endoneurium. Sir V. Horsley found no change in the vessels, but change in the nerve elements. Krause found here and there thickening of the nerve-sheath, accompanied in one case by thickening of the nerve-fibres; in all cases the arteries were normal. Thus, considering that the material for examination was obtained by twisting the nerve from the canal, the microscopical changes were surprisingly small, and of little pathological importance.

Several observers have examined the Gasserian ganglion, and described changes in the ganglion-cells. But slight changes, such as pigmentation, are common after middle life, and in no case have observations with newer methods of nerve-cell staining been published. I examined a ganglion (removed by Mr. Jonathan Hutchinson) by Nissl's method; it shewed nerve-cells so perfect that they could be used as standard specimens of normal staining of the cells of the ganglion by this method. There was, perhaps, some thickening of the periganglionic tissue, but this was doubtful. Thus as yet the pathological lesion at the bottom of this disease has to be discovered.

*Treatment.*—(a) *Drugs.*—The drugs which have been recommended for this malady are innumerable; but the favourable effects attributed to many of them are probably due to a confusion between the major and minor forms of the disease. Large doses of quinine once a day have been recommended, and in the earlier stages certainly seem to have some effect. The antipyrin group has a palliative effect, even in



comparatively late stages of the disease. Salicylates have a similar effect in some cases. Two drugs, gelsemium and butyl-chloral, definitely ease the pain in the earlier stages, and Sir V. Horsley states that if gelsemium is pushed to produce its toxic effects (one dram every two hours), the patient is relieved, even in the later stages. He states that no relief is obtained until a feeling of sickness with numbness in the extremities of the fingers comes on; relief so obtained is, however, but temporary. In lighter cases opium often gives definite relief, but it tends to increase the constipation from which these patients so commonly suffer. Morphine is only a palliative, and so great is the danger of establishing a morphine habit that Krause forbids its use altogether; cocaine is in this respect even worse than morphine.

(b) *Local Applications*.—Counter-irritation over the painful spots, or the application of the actual cautery, may afford temporary relief. In the same way a paint of equal parts of camphor, menthol, and chloral rubbed up together, menthol in oil, or aconite ointment, may give relief in the earlier stages; but later in the disease they are absolutely without effect.

The application of ethyl-chloride spray, such as is commonly used in minor surgical operations, will also give relief for a time, even in severe cases, and is worth a more extended trial where the paroxysms occur once or twice a day only. The skin of the face should be first protected with a thin coat of grease, and the eye carefully guarded.

(c) *Galvanism*.—At one time the constant current, with the anode resting on the painful point and the kathode on the neck, was considered a valuable cure in trigeminal neuralgia. This error undoubtedly arose from a want of discrimination between neuralgia major and the minor forms. This method of treatment should always be tried, but it rarely affords more than a temporary alleviation, if any. Sir V. Horsley mentions a striking case (which I had an opportunity of seeing); a sufferer from a tolerably severe major neuralgia, who had come into the hospital for operation, was cured, at any rate for a considerable time, by a three weeks' application of the constant current.

(d) *Climate*.—A quiet life in a warm, sunny climate seems to benefit many of these patients, but does not cure the cases which have already become severe. Many patients are undoubtedly worse by the sea; and, as in some cases of brachial neuritis, sea-bathing often increases the paroxysms.

(e) *Operative*.—The minor operations, such as resection or nerve stretching, are to be looked upon as no more than a profound kind of counter-irritation. For the details of these operations Krause's work or some textbook of surgery must be consulted. They afford relief for a considerable time in suitable cases, especially where the pain lies completely within the territory of one branch of the nerve; but ultimately the pain returns in nearly every case.

Prof. Rose attempted to reach the Gasserian ganglion at the base of the skull, and performed several operations by his method. But it was

not until Krause and Hartley independently performed what is now known as the Krause-Hartley operation that excision of the ganglion became so far practicable as to need mention in a textbook of medicine. The operation is shortly as follows:—

A flap is turned down over the temporal fossa with its base at the zygoma. Krause forms an osteoplastic flap; he then enlarges the opening until the lower and anterior third of the temporo-sphenoidal lobe has been laid bare, when, if the opening is of sufficient size, the temporo-sphenoidal lobe is seen covered by dura mater. The dura mater is next detached from the floor of the middle fossa of the skull, and the temporo-sphenoidal lobe, covered by dura mater, is held up with a retractor. Sir V. Horsley insists that the method of raising and moulding the temporo-sphenoidal lobe is of extreme importance to the subsequent condition of the patient, and he prefers to use a mechanical elevator fixed to the skull rather than entrust it to an assistant. Krause ligatures the middle meningeal and then divides it; but Sir V. Horsley plugs the foramen spinosum. The foramen rotundum and ovale now come into view. The cavum Meckelii, in which the ganglion lies, is now opened, and the ganglion is freed as far as possible. The borders of the sensory root are clearly defined. It is then freed and drawn upon with forceps so as to extract it completely from the pons. The root and ganglion are turned forwards, and the middle and inferior divisions of the trigeminal cut close at their foramina. The ophthalmic division is divided close to the ganglion (some of the ganglion is left attached to the stump) in order not to injure the fourth and sixth nerves which lie close to it. Those who have never seen this operation cannot realise how clearly the parts can be seen and individually dealt with. Mr. Jonathan Hutchinson, junior, has modified this operation by removing the second and third divisions only. As the ophthalmic division of the trigeminal remains in connexion with the central nervous system, the eye remains sensitive and escapes the risk of so-called “trophic” disturbance. In most instances this portion of the nerve is not the primary seat of pain, and in such cases Hutchinson’s operation can be strongly recommended.

The wound should heal by first intention, and no unsightly scar be left. The movements of the jaw are of course impaired, but not to such an extent as materially to interfere with the patient’s comfort. Krause has performed thirty such operations, Hartley four, without a death. Sir V. Horsley has operated on more than 250 cases with two deaths only. The first was performed fifteen years ago, and in no case as yet has the disease recurred on the operated side, provided the ganglion has been entirely removed. Thus we seem at last to have found a means of cure for the most terrible of all diseases.

But although the mortality from the Krause-Hartley operation has fallen to insignificant proportions in the hands of skilled operators, it still remains a serious surgical procedure. Schlösser, therefore, suggested in 1903 that the affected branches of the nerve should be destroyed by the injection of alcohol at the point where they leave the base of the

skull. This method has also been used by Sicard in France, and by Dr. Wilfred Harris and by Dr. Purves Stewart in this country. A hollow needle about 1·5 mm. in diameter is thrust through the cheek, following definite landmarks, until the foramen rotundum or the foramen ovale is reached. Then a solution of absolute alcohol, with or without eucaïne or stovaine, is injected around the nerve. Most operators recommend that the patient should not be anaesthetised, as the pain produced when the nerve is reached by the needle is a valuable guide. After the first outburst produced by the injection pain disappears for ten months or more, and in some cases is said not to have returned. The area on the face supplied by the injected branch should become insensitive to the same extent as if the nerve had been completely divided.

**Neuralgia due to Organic Lesions of the Trigeminal Nerve, or of its Roots.**—Certain neuralgic pains which accompany organic lesions of the nerves or nerve-roots must be briefly mentioned here, not because they come within the true scope of this article, but because the diagnosis between them and neuralgia major is often extremely difficult during life.

Tumours of the cranial nerves not infrequently cause intense neuralgic pain radiating over the territory supplied by the fifth nerve. At other times the pain, though paroxysmal and aching in character, is local, and not referred along the course of the nerve. In both cases, however, there is usually distinct loss of sensation over the area to which the affected branch is distributed. The root of the fifth nerve is not uncommonly invaded in tumours growing from the meninges. Krause mentions a case of one of these tumours, around the root of the fifth nerve in a woman, which caused pain so exactly resembling neuralgia quinti major that he operated and successfully removed the ganglion. Fifteen days after the operation she complained of headache, the wound reopened, and finally, after a second exploratory operation, she died. A cholesteatoma of the arachnoid the size of a walnut was found lying in the middle fossa of the skull. Krause makes no mention of the presence or absence of anaesthesia; but in the cases I have seen of a similar pathological condition the loss of sensation was definite. In one of them, in which the mass was malignant, the pain was characteristically neuralgic, but it occupied the whole of one-half of the face. In the second case a growth of small size on the root of the fifth nerve caused the headache, vomiting, and optic neuritis of a cerebral tumour, together with the progressive anaesthesia of the face so characteristic of a lesion of the trigeminal root. Without testing the sensation of the face the former of these closely simulated neuralgia major, the latter an ordinary cerebral tumour. Thus before operation in every case of neuralgia it is well, if possible, to take the opportunity of a period of freedom from pain to test the face carefully for anaesthesia, and to consider the possibility that symptoms might be due to an undiscovered neoplasm.

Tumours of the skull, especially gummæ (nodes), cause intense neuralgic pain apart from implication of the meninges. The anterior part of



the temporal fossa is a not uncommon situation for a gumma. In this position it causes neuralgia over the whole of the temporal fossa, accompanied by marked tenderness of the superficial structures, not only over the actual gumma itself, but over a wide area in front of it, spreading out above and in front somewhat like a fan. This area corresponds to the distribution of the ascending branches passing from the deep parts of the fossa forwards and upwards to the scalp. It does not correspond to any area or combination of areas of referred pain such as are shewn in Fig. 76.

The outburst of herpes ophthalmicus, like herpes zoster, is frequently preceded by severe neuralgic pains, which usually subside somewhat after the rash has come out, giving place to intense soreness due to the condition of the skin. Sometimes, especially in elderly people, or in those broken down in health, pain follows the rash, pain of agonising intensity and typical neuralgic character. This pain is confined to the area occupied by the eruptions, and is most marked in those portions of the skin where the scarring is deepest (*vide* p. 480).

Some time after a fracture or injury to the skull neuralgic pains may arise apart from neurasthenic or hysterical states. In a case in which there had been a compound fracture of the centre of the frontal bone intense neuralgia came on, in attacks of considerable frequency, lasting for a week or more at a time. This pain, though unrelieved by trephining, was probably due to adhesions between the meninges, the scar, and the skin. In another case an intense neuralgic headache, limited to a spot two inches in diameter over the temporal fossa, followed a direct blow received in hunting. There was no pain elsewhere, and the patient was in no sense of the word neurasthenic. The pain was accompanied by intense tenderness, both superficial and deep, limited to this small area only; and, although it throbbed and darted, it did not radiate elsewhere. Gunshot injuries of the skull are said occasionally to produce somewhat similar results; I have, however, no experience of such injuries.

**Neuralgia Minor.**—Within this group are included all those pains which, whether associated with localised pain in some organ or not, have certain characteristics which cause the patient to speak of them as “neuralgia.” It may be that he suffers from an aching tooth accompanied by a shooting or boring pain over some part of the face; or pain in the face may be present without any local manifestation pointing to affection of a tooth or other organ of the head.

In this section are grouped two forms of neuralgia of different origin, but so closely resembling one another, if the pain only be considered, that they have been habitually confused: (i.) Referred visceral pain; (ii.) True neuralgia minor.

(i.) *The Characteristics of a Referred Visceral Pain.*—Many of the pains to be dealt with in this group have not the neuralgic character: they do not give the impression to the patient of shooting along a nerve. Thus, the majority of patients speak of the supraorbital pain produced by some



error of refraction as a headache; some, however, speak of it as a neuralgia. Again, iritis will cause intense neuralgia in the temple and cheek; but if less acute the pain is described simply as aching. Thus it becomes necessary to include in this article on neuralgia all referred pains in the head, for it is a mere matter of severity and of the idiosyncrasy of the patient whether they are called neuralgia or not.

When the pulp of the tooth is exposed to irritation the patient frequently complains of pain in the face. This pain is of greater or less intensity and extent, and comes and goes in paroxysms of varying duration. Each paroxysm is either the single response of the inflamed pulp to stimulation, or is associated with some general state, such as hunger or fatigue. Pain is accompanied by tenderness of the skin and subcutaneous tissue of the face over an area of greater or less extent, according to the tooth affected. Whenever it accompanies referred visceral pain this soreness lies within areas (*vide* Fig. 75) which do not correspond to the distribution of peripheral nerves. During the actual paroxysm of pain tenderness of the skin is not usually perceived; but it remains as a constant and troublesome consequence when the actual sharpness of the pain is passed. Thus the neuralgia itself is intermittent; but so long as the attacks are not too far removed from one another tenderness is persistent. To demonstrate this tenderness, pick up the skin and subcutaneous tissues lightly between the finger and thumb; as soon as the tender spot on the face is reached, the patient will complain that there he feels sore, tender, or bruised. Even a better way, in some cases, is to make light pressure with the spherical top of a common pin: when this is done, provided the hyperalgesia be considerable, the patient may complain that he is being pricked; or, if less intense, that the head of the pin touches a sore, bruised place. In this way one or more areas can be marked out following the lines of those on Fig. 76.

The more prominent the pain the greater will be the tendency of the patient and of his medical attendant to call it neuralgia; the greater the tenderness as opposed to pain, the more likely are they to call it headache or faceache.

Thus the characteristics of a referred visceral pain are—(a) The presence of pain over areas other than those of peripheral nerves; (b) the association of this pain with tenderness of the superficial structures of the head.

(ii.) *True Neuralgia Minor*.—There is, however, a second form of neuralgia minor which differs fundamentally from that just described, although in many cases it stands in relation to discoverable disease about some organ in the head. If, for instance, the periodontal membrane, lining the socket of one of the teeth of the upper jaw, be inflamed, it is not uncommon for the patient to complain of darting pain up the jaw and below the eye. Now such pain is typically "neuralgic" in character, but does not follow the lines laid down for a referred visceral pain. It is, as a rule, unaccompanied by superficial tenderness; but when tenderness is present, the tender area represents the peripheral distribution of the

affected nerve-trunk. An exactly analogous phenomenon appears when the socket of the eyeball is invaded by a growth which does not invade the eye itself. It also appears in innumerable diseased conditions of the jaws and skull.

Such neuralgic pains follow the course seen in neuralgia quinti major; and in the early stages of the latter disease it is often quite impossible to say whether the case will turn out to be of the major or the minor form. We can, however, say definitely at once that, by its distribution and the absence of true superficial tenderness, it is not a true referred visceral pain.

Thus we can formulate the differences between the two groups of pain included in neuralgia minor as follows:—

<i>Referred Visceral Pain.</i>	<i>Neuralgia Minor Proper.</i>
1. Pain usually accompanied by superficial tenderness.	1. Pain not usually accompanied by superficial tenderness.
2. Pain and superficial tenderness follow lines in the nervous system central to the peripheral nerves.	2. Pain (and when present tenderness) follows a distribution representing that of the main branches of the trigeminal.

A characteristic feature of all these minor neuralgias is their tendency to be associated with distinct pain in remote and unaffected organs. This is more particularly the case with referred visceral pain; but it is also a feature of some neuralgias following a peripheral distribution. Thus, glaucoma may cause the teeth of the upper jaw to ache and be tender to percussion, exactly as if they were affected with periodontitis. Exposure of the pulp of a molar tooth in the lower jaw may cause such intense pain as to mislead both patient and physician into thinking that the ear is diseased. I have once seen a perfectly healthy membrana tympani incised under such conditions for the relief of pain that entirely ceased with the destruction of an exposed nerve in the second molar of the lower jaw. In a second case, in which exploration of the mastoid was suggested, all pain and tenderness disappeared with removal of a carious lower molar tooth. Malignant disease of the lateral border of the tongue causes pain in the ear; and I have seen a case in which much valuable time was lost owing to the patient's conviction that he was suffering from earache only. Again, pain produced by one tooth is particularly apt to be referred to another in the same or the opposing jaw. This reference, in my experience, is very rarely made to a tooth of the opposite half of the jaw.

Associated with both the referred visceral and the peripheral nerve form of neuralgia are certain interesting reflex effects. Referred pain from an exposed pulp in the upper jaw will sometimes cause conjunctival injection, or a reflex flow of tears. Salivation is also a well-known accompaniment, especially of pain of dental origin. Tomes mentions a case in which by touching the exposed nerve of a first upper molar tooth

he could at will produce injection of the conjunctiva, a profuse flow of tears, and an outpouring of saliva. I have seen pin-point pupils dilate to their normal size on the removal of a tooth that had caused persistent neuralgia from periodontitis.

All these minor neuralgias are remarkably affected by general states of the body. They are usually at their worst during hunger or fatigue, and improve or disappear to a remarkable degree after a meal or a night's rest—except, of course, in cases in which the mastication of food stimulates an exposed pulp. Alcohol in most cases causes a marked improvement; unless, again, the pain be due to a collection of pus at the root of a tooth, in which circumstances the throbbing pain, so characteristic of this condition, may be increased by the alcoholic stimulation of the cardiovascular system. Of the effect of heat and cold within the mouth, when the neuralgia is due to affections of the teeth, I shall speak later. When the neuralgia is a true referred visceral pain—for example, from a tooth with an exposed pulp—sudden alterations in the temperature of the surrounding air are in all cases unpleasant. Thus, if a patient go from a warm room to the cold winter air the pain is increased, or a fresh attack induced; but in most cases a continuous sojourn in the cold outer air is followed by a distinct diminution of the pain, or even by its disappearance. A return to the warm atmosphere of a room starts a fresh attack at once, which does not, as a rule, disappear, as was the case in the cold air. An attack nearly always comes on as the patient becomes warm in bed, and such patients are often at their worst when sitting by a fire. A clergyman, who, until his teeth were removed, suffered for years from neuralgic pains, told me that for this reason he could never visit his parishioners during the winter. On the other hand, the form of neuralgic pain which is due to periostitis, or periodontitis, is decidedly increased by exposure to cold air, and is usually lessened by sitting over the fire, "or basking the face."

Of all general states of the body that have a profound influence on these minor neuralgias, anaemia is perhaps the most distinct. A patient may be anaemic, and yet suffer from no pain or tenderness. But as soon as some cause for referred pain is present, widespread and diffuse neuralgias make their appearance out of all proportion to the original focus of disease. In an anaemic person menstruation, hypermetropia, or caries of a tooth may cause widespread pain and tenderness of the head and neck. A similar effect is produced by that cachexia which in some cases precedes, by a considerable period, the specific manifestations or signs of pulmonary tuberculosis. Menstruation greatly increases this tendency for all these neuralgic pains to spread widely, especially during the week preceding the flow. Pregnancy, again, is frequently accompanied by facial neuralgia, possibly owing to the readiness of the teeth to decay during gestation. A sudden rise of temperature will frequently produce an increase in a pre-existing neuralgia, especially if it be of the referred visceral type. But in some cases a sudden rise of temperature will produce widespread pain and tenderness of the scalp



without our being able to recognise any area of primary disturbance. This condition is produced most easily by epidemic influenza; in this disease the patient complains of pains all over, and especially in the head. Careful examination shews that in many cases these pains, like referred pains, are associated with tenderness of the superficial structures of the forehead and scalp. Sometimes an attack of influenza will leave behind it persistent neuralgic pains which may belong to both the visceral and peripheral nerve types.

Abnormal mental states, neurasthenia, and hysteria also intensify these minor neuralgias. These will, however, be dealt with later, as more frequently they generate the neuralgia.

One thing that has tended to keep up the belief in the substantial existence of neuralgia as a disease has been the effect of treatment directed not to the cause, but to the pain itself. A leech or blister may relieve the pain for a considerable time, even though it be definitely referred from some visceral lesion. Thus, a leech applied over the temples has a profound effect on the referred pain and tenderness of acute glaucoma. Violent counter-irritation seems to produce some effect upon the nervous system, which prevents the generation of these pains, even though the focus of disease be untouched. Thus, I have seen an operation on the skull, in which nothing was done to the nerve, abolish the most profound neuralgia major for nearly a week. A purge or a full dose (5 to 8 grains) of quinine taken at night will often abolish a neuralgia definitely due to the exposure of an inflamed dental pulp. But the results of such treatment are extremely misleading, and in spite of the apparent cure the focus of disease should always be looked for carefully.

In neuralgia quinti major we saw that heredity played but a small part. With these minor neuralgias, on the other hand, it is extremely common to find a tendency to nervous or mental disease. In some cases it would even seem as if a direct tendency to neuralgic pains may be inherited. But since we no longer look upon neuralgia as a uniform disease the question of its heredity is of but little interest.

*Neuralgia Minor secondary to Diseases of the Teeth.*—The first stage of caries of a tooth consists in the removal of the enamel and excavation of the underlying dentine. During this process pain may or may not be present, but can generally be elicited by stimulation of the affected tooth. The most effective stimuli in this condition are heat and cold; for in many cases, even where the carious part of a tooth can be cut away without pain, a jet of hot or cold water upon the exposed dentine will produce a twinge of pain. As long as the pulp-cavity is not exposed the pain remains local, and the patient suffers simply from toothache, pointing to the peccant tooth as the source of his trouble. The pain may dart and shoot, but the darting and shooting are practically confined to the aching tooth. Local stimulation produces local pain and neuralgia is absent. As soon as the pulp-cavity is exposed the pain alters in character and distribution. It may start in the affected tooth and shoot into the face, forehead, neck, or ear. Each stab of pain lasts a few moments, only to be followed more or



less rapidly by a second twinge. Eating or any other such act stimulates the exposed pulp, increases the pain, or starts a paroxysm. Hot and cold fluids taken into the mouth usually much increase the pain.

On testing the face or neck within the areas affected by this neuralgia, more or less tenderness of the skin and superficial structures will be found over areas more or less corresponding to those shewn in Fig. 75. On the face the tenderness is superficial; but parts of the jaw, mouth, and tongue may be tender at a distance from the affected tooth, owing to their participation in the area affected. Thus teeth at a distance from that affected may ache and be tender to the touch.

Many patients are aware of the presence of this tenderness, and state that they first feel the darting and shooting pain, which seems to leave a soreness behind it. When such a tender area on the face is tested for tenderness it is not uncommon for the patient to complain that a touch within its limit seems to make the pain in the tooth worse. This tenderness does not arise until the neuralgia has lasted several hours, and it usually disappears, without further treatment, within twenty-four hours of the removal of the tooth. But in a few cases the pain and tenderness spread widely, extending even to the arm; such cases are best treated by cleaning out the wound produced by the extraction, and applying some preparation of cocaine. The pain usually lasts about a week or ten days in the acute form, and then subsides gradually. It may happen that when the patient comes under observation the pain has ceased for many hours; in such cases tenderness will probably be absent, and yet from the account he gives of the nature and cause of the pain, it is certain that it was a referred visceral pain from some tooth. For instance, pain in the ear represents the maximum point of the hyoid area (*vide* Fig. 76); this area is peculiarly associated with the teeth of the lower jaw from the second bicuspid backwards. Thus we can argue that the patient who complains of referred pain in the ear is probably suffering from irritation of one of these teeth, although the pain may be unaccompanied by tenderness at the time of his visit.

Where the pulp becomes fibrous or calcareous it is not uncommon for the nerve, or part of the nerve, to retain some vitality in one root, although the pulp and nerve of the other root be dead. Irregular calcification, with the formation of pulp-stones, frequently leaves some living pulp, and is a potent cause of neuralgia. In all such cases attacks of neuralgia of the referred visceral type accompanied by superficial tenderness are apt to appear from time to time; and it is under these conditions more particularly that the dental origin of the neuralgia is most likely to be overlooked. There is no toothache, but the dying contents of a root tend to light up into activity from some indefinite cause; or the patient's general health deteriorates, and he suffers from a sharp attack of neuralgia which is put down purely to his lowered vitality. The pain passes off under general treatment, and its origin in a tooth remains unsuspected. The presence of superficial tenderness over one or more of the segmental areas of the face should have made the case clear, and directed attention

to certain of the teeth amongst which the affected tooth would have been found.

So long as the pulp or contents of the root are living, inflammation of the cavity of the tooth will produce neuralgie pain of the referred visceral type. After caries has reached the pulp-cavity many different changes can occur. The pulp and nerve become inflamed and reddened, and may die rapidly and steadily. Sometimes this inflammation and death of the pulp take place with extreme rapidity, and four or five hours of agonising pain are followed by perfect peace. Sometimes, however, death takes place much more slowly; one part, or the whole of the pulp in the chamber of the tooth, may die, and with it the nerve in one or more roots, yet the nerve in one root may remain alive and potent for harm for a long while. Again, the inflammation and death of the pulp may go on slowly under a cap of sodden dentine. Under all these conditions referred pain, accompanied by more or less superficial tenderness over the segmental areas of the face, is almost certain to make its appearance at some time or another.

The exact innervation of each tooth from the segmental areas seems to vary somewhat, but the following table gives the approximate supply, as it has been worked out at present :—

Upper Jaw.		Lower Jaw.	
Incisors . . .	Fronto-nasal.	Incisors . . .	Mental.
Canine . . .	Naso-labial.	Canine . . .	„
1st Bicuspid . .	„	1st Bicuspid . .	„
2nd Bicuspid . .	Temporal or maxillary.	2nd Bicuspid . .	Doubtful.
1st Molar . . .	Maxillary.	1st Molar . . .	Hyoid.
2nd Molar . . .	Mandibular.	2nd Molar . . .	„
3rd Molar . . .	„	3rd Molar . . .	Superior laryngeal or hyoid.

When the pulp and nerve are dead a tooth may still be a source of pain of neuralgie character, owing to inflammation of the periodontal membrane or abscess about the root; but this pain is usually local and situated in the tooth itself. If, however, the pain shoot from the tooth into the jaw and neuralgia appears, the distribution and the accompaniments of the pain in the vast majority of instances differ fundamentally from those produced by inflammation of the pulp: it closely follows that already described in neuralgia quinti major, and superficial tenderness over the visceral segmental areas of the face is extremely rare. A tooth in this condition frequently seems as if it were “too long,” or “longer than the teeth around.” Intermittent pressure on such a tooth as in chewing causes pain, but steady pressure relieves the pain for a while. The patient frequently pulls at such a tooth, moving it backwards and forwards for the sake of the subsequent ease produced by this momentarily painful manipulation. Cold water taken into the mouth usually eases the pain, but hot water nearly always increases it. Pressure sometimes causes a

twinge of pain which travels beyond the limits of the tooth; thus, when the periodontal membrane is inflamed, pressure on a canine may cause a neuralgic pain which darts into the upper jaw and below the eye. Pressure on a lower bicuspid causes a pain to run along the jaw and affect all the teeth behind; this pain, however, does not come out upon the face, as with the upper canine. Thus in neither case does the pain follow the lines of segmental areas, but we see at once how closely it follows the distribution with which we are familiar in cases of neuralgia quinti major.

This neuralgic pain may arise without any conscious stimulation of the tooth, and the differential diagnosis then becomes of great importance. It can only be made by noting the direction of the pain and the absence of superficial tenderness.

Periodontitis or alveolar abscess may produce a pain away from the tooth affected in two ways. In the instances just given branches of the nerve (not the nerve-endings to the pulp) are probably involved in the inflamed tissue; pain then radiates up the nerve exactly as pain radiates up the ulnar when the divided peripheral end has been caught in scar tissue. But periodontitis can cause radiating pain in another manner. Suppose a non-erupted dead wisdom tooth to lie below the gum, and to set up inflammation around it, which involves the trunk of the nerves to the teeth in front: under such conditions the pain radiates along the branch of the nerve, and is felt in all the teeth of the lower jaw. This phenomenon corresponds to the radiation of pain to the little finger produced when the trunk of the ulnar nerve is affected by inflammation about the elbow-joint.

Thus in tracing the dissolution of a tooth we first find local pain and tenderness due to early caries and exposure of the dentine with a healthy pulp; then referred pain of the visceral type, accompanied by more or less superficial tenderness, the consequence of chronic inflammation and destruction of the pulp tissue; and, lastly, after the death of the pulp, local pain and tenderness, with or without neuralgia, appear in consequence of periodontitis or abscess formation at the root. Such pain follows the distribution of peripheral branches of the trigeminal and not that of segmental areas.

Bearing in mind these facts we cannot wonder that pyorrhoea alveolaris is a frequent cause of widespread and intractable neuralgia. Suppuration in the sockets of the teeth irritates the nerves as they leave the roots, and causes pain resembling that evoked by irritation of any fine branch of the trigeminal. Suppuration may spread inwards to the pulp through the terminal canal, and the neuralgia with tender areas on the face be added to that due to the irritation of nerve twigs.

Before concluding this section I must allude to a curious form of neuralgia often accompanied by all the signs of widespread referred visceral pain, due apparently to what is known as "cross-bite."

*Neuralgia Minor secondary to Changes in the Eye.*—Errors of refraction do not commonly give rise to neuralgic pain of any severity. Though



an extremely fruitful source of headache, the pain so produced is rarely paroxysmal, and its steady aching character leads patients to speak of it more often as a headache. Yet if the patient become anaemic, or the general health fail, this headache may present characters which lead the patient to complain of frontal neuralgia. It is necessary, therefore, to consider shortly the position and peculiar features of the headache due to errors of refraction. If asked to point out the situation of the pain, the patient usually places his right hand over the forehead, with the hypothenar eminence over the centre of the right eyebrow, and the second phalanges of the fingers over the centre of the left eyebrow. This position of the hand has led to the common statement that the headache is situated over the centre of the forehead; but the patient himself states that the headache is "over the eyes"; and if asked to point with two hands to its position he will place the tips of the fingers of each hand over the centre of each eyebrow.

This headache, as is usual with referred pains of visceral origin, is associated with more or less superficial tenderness, which, in errors of refraction, lies over the mid-orbital area (*vide* Fig. 75). As a rule only the maximum of this area is present; but occasionally, especially if the patient be seen immediately after reading or sewing, the whole area may be tender. This headache comes on in the morning as soon as the eyes are opened; and, unless the patient engage in near work, it gradually wears off during the day. It is intensified by reading or sewing; it disappears if the eye is put under atropine, and is worse over the eye with the greater error of refraction, provided that this eye be not amblyopic.

Astigmatism of all kinds is a fruitful source of headache; and of the errors of refraction, hypermetropic astigmatism is the most likely to cause headache. For whilst a simple error of  $+1D$  or  $+2D$  can frequently be neglected, an astigmatic error of  $+1D$  will not uncommonly produce definite pain and tenderness.

Simple myopia, however high the error, causes no such headache and tenderness. The myope sometimes complains of a tired, aching feeling over the forehead, which is never, either in intensity or character, the least like neuralgia. It is not accompanied by tenderness, and is always absent on awaking from a night's rest. In those uncommon cases, however, in which myopia is associated with spasm of accommodation, referred visceral pain of considerable intensity and wide distribution may be present. It entirely disappears if the eye be put fully under atropine.

The gradual breakdown of accommodation which accompanies the establishment of presbyopia in a hypermetropic person of about forty, is not infrequently associated with very considerable discomfort. This entirely ceases when presbyopia is fully established, and headache ceases as vision fails for near objects. If, moreover, the patient is a woman, the association of the climacteric with the presbyopic failure may be responsible for much troublesome pain of the referred visceral type.

In all these conditions pain and tenderness originally lie over the



mid-orbital region of the forehead ; but if severe they tend to spread both forwards to the middle line of the forehead and backwards into the temporal fossa, and upon the vertex.

Usually the presence or absence of a headache due to errors of refraction depends directly upon the extent to which the eyes have been used. But in some cases the headache assumes a curious paroxysmal character. The patient may use his eyes continuously for near work, yet suffer from one or more attacks of headache only during the week. Such headaches are, however, extremely severe, are sometimes accompanied by vomiting, and not uncommonly interrupt the patient's work. They are then called migraine ; but they differ from true migraine in the presence of marked superficial tenderness of the referred visceral type, in their bilateral distribution, and in the absence of any of the higher visual phenomena such as fortification figures.

When the deeper layers of the cornea are affected, as, for instance, by a deep or ragged ulcer, or if the depth of the anterior chamber of the eye be increased by disease, pain of a definitely neuralgic character may come on. The pain and tenderness are situated primarily over the fronto-nasal area, and the pain down the inner side of the nose is sometimes very decided. Later, if the lesion be very severe or the patient in ill-health, both pain and tenderness may spread backwards to the temple and scalp.

Of all the diseases of the eye iritis and glaucoma produce the most definite neuralgic pain. In both diseases the pain is situated primarily over the temporal and maxillary regions, but may spread forwards up to the middle line, or backwards and upwards to include the vertex. In iritis this neuralgic pain may be severe ; but in glaucoma it may become agonising, and is frequently accompanied by vomiting and considerable prostration. In acute glaucoma the pain in the eye itself is so acute that, except from gross carelessness, there is no chance of an error in diagnosis ; but in chronic glaucoma the neuralgia (referred visceral pain) may become so prominent a feature that its dependence on disease of the eye remains unrecognised. I once saw a patient who had been treated for intractable attacks of neuralgia for a month before it was recognised that she was suffering from glaucoma ; by this time the sight of the affected eye was irretrievably lost. During an attack of glaucoma it is not uncommon for the teeth of the upper jaw to ache on the side affected ; this is due to the frequency with which the maxillary segmental area becomes tender in consequence of rise of tension within the eyeball. If the pain and tenderness spread forwards to affect the frontal area, the teeth of the upper jaw ache up to the middle line ; if they spread back, as is not uncommon in an attack of glaucoma, the teeth of the lower jaw may ache also. Occasionally the teeth affected are tender to percussion, as if affected with periodontitis. That this tenderness is reflex, and not due to any actual change in the sockets of the teeth, is shewn by the daily variation in the position and number of the tender teeth, coincident with changes in the condition of the eye, and by its occurrence in an edentulous jaw.

Changes in the retina and optic nerve are, as a rule, unaccompanied by pain. But there is a peculiar form of primary optic atrophy, due to some unknown cause, in which the progressive loss of vision is marked by severe pains in the head which are invariably called neuralgia. These pains are accompanied by soreness of the scalp. There are no associated signs of disease in any other part of the body or of the central nervous system. The three cases I have seen were all in women, and vision was ultimately lost completely. Beyond this point the disease, whatever its nature, does not seem to progress. Thus neuralgia of the forehead or scalp, with progressive loss of vision, should always lead us to look to the tension of the globe and the condition of the optic nerve.

Orbital growths, on the other hand, cause pain which is either local or follows the nerve, and is unaccompanied by tenderness of the forehead or scalp.

*Neuralgia Minor produced by Disease of the Ear.*—Pain produced by lesions of the auditory meatus, from its opening to the membrana tympani, is local, though frequently severe. If, however, the membrana tympani or middle ear be affected, the pain will be referred to some point at a distance from the source of irritation, and may be accompanied by superficial tenderness. It is particularly prone to all those characters which lead the patient to speak of it as neuralgia. During suppuration in the middle ear, before perforation of the membrana tympani, the pain is intense; it is situated over the side and top of the head (vertical and temporal areas), and in and behind the ear (hyoid area). The former ceases when the discharge appears, but the pain and tenderness over the hyoid area usually remain. This persistence of tenderness over the hyoid area is probably due to inflammation of the membrana tympani, which continues to cause referred pain after the tension in the middle ear has been relieved. A similar set of symptoms may be caused by the blocking of an already established opening in the membrana tympani.

Thus for practical purposes the hyoid area is that which is most commonly the seat of pain and superficial tenderness in ear disease. The vertical and temporal areas of the scalp, which might lead to errors in diagnosis, are only present when tension in the middle ear rises to such an extent that the aural origin of the pain can scarcely be overlooked.

*Neuralgia Minor secondary to Diseases of the Tongue.*—It is well known that malignant disease of the tongue may cause pain in the ear, or over the back of the head, in addition to the pain in the tongue itself. Gumma of the tongue may also cause pronounced neuralgic pains of the visceræ type. If the disease affects the anterior part of the tongue, pain is felt over the spot where the mental nerve rises through the deeper structures of the jaw to supply the skin (the maximum of the mental area). If the lateral part only of the tongue is implicated, the patient complains of pain in the ear and behind the ramus of the lower jaw on the side affected. In such cases the hyoid area is tender. But as the disease is rarely confined to one part of the tongue, tenderness is generally found in some other area besides the hyoid. When the dorsum of the tongue is

affected, the pain may be situated in the occipital region, and take the form of occipital neuralgia. But the presence of superficial tenderness at once reveals its true nature as a referred visceral pain.

Thus lesions of the tongue are associated with tenderness over three main areas: (a) the mental area in disease of the anterior portion; (b) the hyoid area in disease of the lateral portion; and (c) the occipital area, when the disease is situated over the dorsum.

Diseases of the tonsil frequently cause pain behind the jaw, associated with superficial tenderness over the hyoid area. Though severe, this pain cannot possibly lead to any confusion.

*Neuralgia Minor due to Diseases of the Nose.*—Few nasal affections are painful, and even in those that cause pain it is rarely acute enough to be spoken of as neuralgia. In inflammatory conditions of the olfactory portions of the nose and frontal sinuses, pain may appear over the fronto-nasal and mid-orbital areas of the forehead; but pain from this cause rarely reaches the intensity of a neuralgia, unless the patient be highly neurotic or in a low state of health. Under such conditions operations directed to the removal of the primary cause do not always cure the pain.

With syphilitic disease of the bones of the nose much pain may be present. I have seen but few cases of this pain in its acuter form, and cannot say therefore whether it follows the lines of a referred visceral pain or not. It is situated over the forehead and over the eyes.

In many affections of the brain intense pain is felt which, till the nature of the disease is discovered, is not infrequently called neuralgia. Such pains, though in some cases neuralgic in character, do not come within the scope of the present article (*vide* art. "Cerebral Tumour," Vol. VIII.).

**Neuralgia and Headache secondary to Disease of the Organs within the Thorax and Abdomen.**—It has long been known that disease of the abdominal and thoracic viscera can cause pain in various parts of the head. But it was not until the discovery of the importance of superficial tenderness that the headache due to general diseased states, and those due to direct reference of visceral pain from the thorax and abdomen to the head, could be distinguished. In this section I shall treat of the latter kind only, reserving those pains in the head which are due to general diseased states for the succeeding section (p. 564).

Any organ of the chest and abdomen may, under favourable conditions, cause visceral pain referred to the head. These pains in the head, like all other visceral pains, are associated with scalp tenderness. The head is not mapped out into areas, each of which represents some organ of the thorax and abdomen, as some would have it, but the areas on the head are segmentally coupled with those on the body, and thus stand indirectly only in relation with any particular organ in the body. For instance, the temporal area of the scalp is usually associated with the seventh dorsal area, which runs round from the back, below the angle of the scapula, to the epigastrium. Now, speaking broadly, it is



quite immaterial, for the production of temporal headache with tenderness over the temporal area of the scalp, whether the disease be phthisis destroying the base of the lung, gastritis, certain forms of mitral disease, or anaemic gastralgia. The only necessary condition is that one of these diseases should produce a certain segmental area of cutaneous tenderness on the surface of the body (seventh dorsal), when the temporal area will appear irrespective of the nature of the disease.

The degree to which these pains in the head intrude on the patient's consciousness varies greatly. Thus, sometimes he is quite unaware that the scalp is tender, and the associated tenderness is only discovered by examination. Again, he may be aware of the soreness of the scalp, but he complains not of pain, but simply of tenderness over certain areas of the skin when he brushes his hair. He may, however, complain of headache, or finally of shooting neuralgic pains which, when they pass off, leave behind them a feeling of intense soreness. Thus, the patient's indications give a clue solely to the intensity of this associated phenomenon. The acuter the pain in the body the more intense and "neuralgic" is the pain in the head likely to be. Thus, in some cases of aortic disease, especially those with paroxysmal attacks of referred pain (secondary angina pectoris), patients complain bitterly of shooting and darting pains in the forehead and side of the head.

**Neuralgia secondary to General Disease.**—(a) *Anaemia*.—Simple anaemia, as such, is not a cause of neuralgia; for in cases of pernicious anaemia and of profuse haemorrhage we observe no tendency to these pains. However, a referred visceral pain once started in such a patient will spread widely. The majority of young girls suffering from anaemia (chlorosis) suffer from widespread neuralgias of the referred visceral type associated with widespread areas of superficial tenderness. As, however, in a certain proportion of quite definite cases of this disease neuralgia is absent throughout, it seems rational to suppose that when neuralgia is a prominent feature it arises from some visceral disturbance, however slight, which, owing to the diminution of resistance within the nervous system, spreads widely and reaches an intensity out of all proportion to the original cause.

(b) *Diabetes*.—Neuralgias are common in diabetes, especially about the jaws and the face. These may possibly be due to the frequency with which the teeth decay, especially in the severe cases of diabetes. The presence of these pains has been said to vary with the quantity of sugar in the urine, but of this I have no experience. Whatever the cause of these neuralgic pains about the face, there is no doubt that diabetics are prone to painful affections of the neuralgic kind, possibly due to neuritis, as is shewn by the frequency of sciatica in this disease.

(c) *Malaria* is apt to produce the well-known "brow ache," now so little seen in this country. In the few cases I have seen this pain preceded the paroxysm, and in one case seemed to alternate with the attacks or to replace them. It closely resembled the frontal pain of influenza.



(d) *Rheumatism* is frequently cited as a cause of neuralgia; but amongst the many manifestations of acute and subacute rheumatism (of the kind associated with cardiac disease) there is no special tendency to neuralgias of the head. Even "muscular rheumatism" (of the lumbago type) is not associated with neuralgia of the scalp or face. That these pains are relieved by salicylic acid and its derivatives is no proof that rheumatism is a factor in their production, for this drug relieves other pains which are obviously not of rheumatic origin. Thus to say that rheumatism is the cause of any particular neuralgia is but a cloak for our ignorance, and is particularly pernicious in that it tends to relieve the observer of further search for a cause. I have even heard the referred pain of an acute iritis called "rheumatic neuralgia." Now, whatever the cause of the iritis may have been, the pains it produced were exactly what we should expect from acute inflammation of the iris, and these, as such, should have attracted attention to the eye at once.

(e) *Hysteria and other Mental States*.—Neurasthenia and hysteria are fruitful sources of neuralgia. The pain so commonly present in the back is associated with shooting pains in the occipital and vertical regions. Such local pains in the head may precede a hysteroid attack, or a true hystero-epileptic convulsion, by some hours or days. After such an attack hysterical patients exhibit intense and widespread superficial tenderness of the whole body, including the head and neck, probably due to the diffusion of visceral pain consequent on the decreased resistance in the nervous system. An exactly similar condition may follow a true epileptic attack in which consciousness is lost, urine passed, and the tongue bitten.

Hypochondriacs and sufferers from insanity with visceral delusions may suffer from extremely local and permanent pains of the head. These pains will be discussed in other articles; but I want to draw attention to certain cases in which an outburst of insanity is heralded by a minor neuralgia exactly similar to that produced by disease of the teeth. In one such patient every possible care had been taken to eliminate any focus of disease in the teeth, yet for a few weeks preceding each relapse he was troubled with definite neuralgic pains exactly resembling those produced by caries of the lower molar teeth. In a second case an outburst of neuralgia was always the signal for a relapse into a condition of violent delusional insanity. All pain ceased immediately when the relapse fully declared itself.

I should like to call attention to a type of paroxysmal neuralgia, almost confined to women, which is not sufficiently recognised in systematic medicine. From childhood the patient complains of "neuralgic headaches," which at first occur three or four times a year, but increase considerably in frequency between the ages of twenty and thirty. These headaches are bilateral, and are not associated with scotomas, fortification figures, or other visual phenomena. The whole head becomes intensely tender, and the patient usually goes to bed in a darkened room some-

times for two or three days. Nausea and dislike of food are present, but the violent cerebral vomiting so common in true migraine is absent. These headaches are strongly hereditary; I have seen grandmother, mother, and daughter with paroxysmal neuralgia of this kind, and know a family in which the condition has occurred widely in four generations. Between thirty and forty years of age the misery of these repeated attacks not uncommonly induces a secondary neurasthenia, and with the consequent diminution of resistance the pain becomes almost constant. In this state I have known the patient commit suicide deliberately. These paroxysmal neuralgia headaches are worse before menstruation, but do not cease with the menopause.

**Treatment.**—The first and foremost rule in the treatment of these minor neuralgias is to find out the organ from which they arise, and to treat the conditions found there. To aid the discovery of this primary focus of disease has been the aim of the previous pages; yet after all we must confess that too often in cases of minor neuralgias the cause eludes us.

It is also of great importance to treat the general condition of the patient, even though the local cause of the neuralgia be already known. For, whatever the cause of the pain, it is always intensified by inanition, cachexia, anaemia, or any general diseased state of the body. Thus, in the case of widespread headache due to hypermetropia in an anaemic person, the anaemia must be treated, as well as the error of refraction.

Wherever the neuralgia is supposed to bear any relation to syphilis or malaria the specific remedies will, of course, be tried before any other treatment is adopted.

The antipyrin group (antipyrin, antifebrin, pyramidon) and aspirin, alone or in combination, have an extremely good palliative effect on the minor neuralgias, and even when they depend on a definite visceral lesion will often completely remove them for a time. Phenacetin, the mildest of the group, in doses of from ten to fifteen grains, will completely relieve a referred visceral pain in the head whatever its origin. The primary minor neuralgias are less amenable to this group of drugs, but generally yield for a time to antipyrin or antifebrin.

Gelsemium and butyl-chloral are invaluable in all minor neuralgias within the territory of the trigeminal, whether they be referred or not. These two drugs, and especially gelsemium, seem to act readily in those cases of primary minor neuralgia in which the antipyrin group is not so effective. Nitroglycerin ( $\frac{1}{100}$  to  $\frac{1}{50}$  gr. three times daily) in some cases relieves these pains.

Bromides are extremely unsatisfactory, except where the pain has spread widely. Strychnine or nuxvomica is often far more efficacious, probably by their tonic effect on the nervous system.

Of local treatment nothing is so good as a small blister, or a couple of leeches, applied to the spot of maximum pain. We do not know how either of these remedies acts, but in most cases of minor neuralgia they

give ease with surprising rapidity and certainty, especially where the pain is referred.

Galvanism is often very useful, the anode being applied steadily over the painful spot and the kathode over the spine.

In all forms of minor neuralgia suggestion has been used, in many cases with considerable success, more particularly in those patients who are not hysterical.

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# DISEASES OF THE VERTEBRAL COLUMN AND SPINAL MEMBRANES

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DISEASES OF THE SPINAL MEMBRANES.



## DISEASES OF THE VERTEBRAL COLUMN AND COMPRESSION-PARAPLEGIA

By Sir VICTOR HORSLEY, F.R.S.

A CERTAIN degree of compression of the cord is caused by various conditions and diseases of the spinal cord with its membranes and the surrounding vertebrae. For the treatment of several of these disease states reference must be also made to the special articles dealing with each.

Compression of the spinal cord gives rise to a very definite group of symptoms, the differential diagnosis of which is often difficult, but now admits of a considerable approach to accuracy.

The subject falls under the following headings :—

I. Seat of origin, and nature of the causes of compression ; II. Symptomatology and diagnosis ; III. Site of the mischief ; IV. Treatment.

**I. Causes of Compression of the Spinal Cord.**—The spinal cord may be compressed by disease or injury of the vertebrae, of the intervertebral discs, of the membranes and tissues in the neighbourhood of the spine, by growths springing from the meninges of the cord, or by intra-theal haemorrhage. Of these, invasion of the neural canal, as a result of tuberculous caries, is the commonest. Next to caries must be placed fracture of the spine ; then new growths ; and lastly, parasites.

From what has just been said it follows that the causes and their nature are best considered under the heads of—(A) the extrinsic ; (B) intrinsic : the plane of separation being the dura mater sheath, or theca, of the cord. The first class, therefore, will consist of extra-theal causes, and the second class of intra-theal.

**A. Extra-theal Sources of Compression.**—The vertebrae are liable to become the seat of the following destructive processes :—

(a) *Tuberculous Disease or Caries of the Spine.*—This disease has three chief seats of origin :—The first occurs just beneath the vertebral bodies at their articular surfaces ; the second seat is the cancellous tissue of the laminae, and, subsequently, the periosteum ; the third is the peritheal tissue. Probably, however, the occurrence of tuberculous disease here is secondary to mischief arising primarily in the bone.

Tuberculous disease of the bodies of the vertebrae produces, as a rule,

an abscess as well as the marked deformity which is referred to on p. 574. When an abscess is present it forces its way down the bodies of the spine, under the anterior common ligament, and then along the fibres of the psoas muscle, provided it takes origin from a point not higher than the middle of the posterior mediastinum. It also extends, however, horizontally backwards, and then meeting in the middle line the opposition of the posterior common ligament, it projects into the neural canal as two lateral swellings, usually of unequal size; these swellings press the spinal cord back against the laminal arches, and compress it laterally also. When the operation of laminectomy is performed these swellings are found as elastic, reddish, rounded eminences at the side of the theca. They are readily opened, their contents scraped and removed, and the cavity disinfected and drained. The proximity of the abscess causes a certain degree of perithecal pachymeningitis.

(b) *Caries sicca* is the next disease of the bone to be considered; by it is to be understood a progressive rarefactive osteitis in which the enlarged spaces in the bone are filled with a deep-red granulation-tissue, the microscopical appearances of which resemble those of a small spindle-celled sarcoma. This is a form of caries of unknown pathogenesis, and may bring about a severe compression of the cord without producing much deformity, or occasionally indeed without producing any; as its name denotes, it is not attended with abscess formation.

(c) *Neoplasms*.—The next commonest cause is *new growth* arising from the periosteum, or from the substance of the bone, and gradually involving the spinal cord by penetrating the intervertebral foramina, and thus encroaching on the space of the neural canal.

The bodies of the vertebrae frequently become the seat of new growth, either of sarcoma or secondary carcinoma. So, too, sarcoma arising in the muscles or tendons, whether primarily or as part of a general sarcomatosis, may likewise produce paraplegia.

(d) *Trauma* may lead to compression in one or other of the following ways:—

(i.) Separation of contiguous bodies of the vertebrae combined with fracture or subluxation—where such subluxation is possible—of the articular processes of the vertebrae, with the effect of allowing the relative positions of the vertebrae to be distorted, and so of causing a narrowing of the neural canal.

(ii.) Crushing of the body of one vertebra, combined with fracture of the laminae and articular processes, so that the cord is compressed by the sharp edge of the body of the lower vertebra projecting into the neural canal, the upper part of the spine being displaced forwards.

(iii.) Displacement of an intervertebral disc, which may be squeezed backwards from its normal position between the damaged bodies.

(iv.) Haemorrhage.

Though it might be expected that, in view of the rich vascular supply of the perithecal tissue, free haemorrhage in the neural canal, as a direct result of trauma, would be common, such is not the case; and



though intra-thecal traumatic haemorrhage is sometimes severe in its effects, and intra-medullary haemorrhage always so, perithecal bleeding is not, practically speaking, a source of compression.

Of other but much rarer sources of compression must be mentioned :

(e) *Aneurysm*.—A very dangerous cause of paraplegia from compression is aneurysm of the descending aorta. This, when situated in the posterior mediastinum, causes erosion of the bodies of the vertebrae, and consequent collapse of the same, if the progress of the mischief be considerable; the disease is very uncommon now, but must always be carefully borne in mind in forming a differential diagnosis. It is to be detected, of course, by the ordinary physical signs of aneurysm, and by the peculiar boring character of the pain. It most commonly occurs in the lower half of the dorsal region (*vide* Vol. VI. p. 633).

(f) *Parasites*.—*Echinococcus* cysts, if they develop retroperitoneally or in the thoracic region, may invade the neural canal in the same way as new growths, that is, through the intervertebral foramina; they may also produce a certain amount of erosion in the bodies of the vertebrae, but do not produce collapse or the same angular deformity as in the case of neoplasms. Deformity may be present, however, as in Cruveilhier's classical case. The pressure effected by hydatid cysts is always very severe, and the consequent destruction produced in the cord, by the ischaemic disturbance of the circulation therein, is but slowly recovered from after laminectomy has removed the cause;—slowly, that is, as compared with the relatively rapid recovery in cases of caries. The treatment, of course, is early laminectomy with, as far as possible, thorough extirpation of the cysts.

B. Intra-thecal Sources of Compression.—(a) *Neoplasms*.—The commonest source of uncomplicated pressure within the dura-matral sheath is some form of new growth situated either outside or inside the spinal cord, and therefore to be considered under these two aspects. (i.) Extra-medullary neoplasms grow most frequently on a nerve-root, commencing chiefly where the arachnoid and pia mater are reflected around the roots at their junction with the intervertebral ganglion. They are either benign, such as fibromas or fibromyxomas, or malignant, such as endotheliomas or sarcomas. The pressure they cause is of necessity very localised. (ii.) Intra-medullary neoplasms are relatively very rare, though gummas in the form of spherical tumours are not uncommon (*vide* p. 868). Simple cysts and syringomyelic cavities occur frequently as sources of intra-medullary pressure. Unquestionably syringomyelia, whether accompanied by gliosis surrounding the cystic space or not, may be confounded in diagnosis with the other conditions now under discussion. At the same time, it is so different in character that it should be easily distinguished from genuine compression of the spinal cord; the cardinal points of difference are undoubtedly the early and patchy occurrence of analgesia in syringomyelia, and the early atrophy of muscles under the rapid and injurious invasion of the anterior cornual centres. Of gliosis accompanying the formation of the

central cystic spaces the extension upwards of the symptoms is perhaps the best indication. In such cases no amelioration can be obtained by operation; but in simple syringomyelia some temporary improvement can unquestionably be gained by tapping the dilated cavity in the cord.

(b) *Pachymeningitis*.—Compression of the spinal cord by pachymeningitis produces clinical symptoms often closely parallel to those evoked by neoplasms. In this condition there is not only greatly raised tension of the cerebrospinal fluid, but also secondary (?) changes in the spinal cord.

**II. SYMPTOMS AND DIAGNOSIS.—Local Conditions of the Spine in Cases of Disease causing Compression of the Spinal Cord.**—*Deformity of the Spinal Column*.—The various diseases which produce compression-paraplegia affect the spinal column very diversely. It will be best, therefore, to group the cases according to whether the disease actually causes a certain amount of physical destruction of the bone, and hence a yielding of the same, so that either the natural curves of the different regions of the spine are exaggerated—for example, the dorsal region becomes kyphotic,—or an aberrant curvature makes its appearance at some one point in the column, when the curvature is definitely angular, or sometimes, in a combination of these causes, it is both angular and lateral.

There is another condition often to be taken into account, namely, that the spine is not infrequently held by the patient in an unusual attitude on account of pain; or, by reason of pain, the natural tone of certain supporting muscles is interfered with, so that the spine automatically assumes a curve resulting from the functional paresis of the muscles in question. It may be stated that in such circumstances the spine usually presents a large kyphotic curve or frequently a lateral flexion.

The conditions under which deformity of the spine is especially to be looked for and expected are (i.) tuberculous caries; (ii.) fracture-dislocation; (iii.) new growths, attacking the bodies of the vertebrae.

The details of these conditions must be sought for in surgical works; but for the purposes of diagnosis attention must here be directed to the fact that, in certain regions of the spine, it is very difficult to detect a deformity which, if harmony with other symptoms is expected, ought inferentially to be present. Thus, in the cervical region it is perfectly possible for a complete fracture-dislocation of the body of the fifth or sixth cervical vertebra to exist without any disturbance of the lines of the cervical spine; and this may occur, and any deformity still be invisible, even when the spines and laminae are denuded of the muscles and ligaments, as in a laminectomy. So too in the lumbar region, extensive tuberculous (non-suppurative) caries, producing the severest paraplegia, may be present without the slightest deformity of the spine.

This is the suitable place to estimate the influence of deformity of the spine in producing compression-paraplegia of the spinal cord. It is



Nerve Root.	Motor.	Sensory.
C. 1.	<div> <div>Small flexors of head.</div> <div>Depressors of hyoid bone.</div> </div> <div> <div>1.</div> <div>2.</div> </div>	<div>C. 1.</div> <div>2. Occipito-parietal region of scalp.</div>



well known that, in the case of tuberculous caries, it is possible to have serious curvature without any apparent pressure effects on the spinal cord. On the other hand, a limited fracture of the body of a vertebra may lead to complete division of the spinal cord. The whole problem is the question whether the neural canal is or is not diminished in diameter. In a caries case, such as that first mentioned, the change in the curvature of the spine is exceedingly gradual; and, unless there be also an abscess-sac pressing backwards, or tuberculous granulation-tissue invading the loose perithecal tissue and fat, practically no mechanical diminution of the neural canal, of any importance, is produced.

On the other hand, in fracture of the spine the neural canal is narrowed very suddenly and severely. It is true no serious degree of narrowing may be found during an operation, or after death, because the bones may spring back; and no doubt they commonly do so as soon as the compressing force, which produced the fracture, is taken off. The sharp angular edge of a fractured body of the vertebra cuts like a sharp-edged instrument in such circumstances, and may hopelessly injure the soft cord by the brief but powerful compression which is exerted. So too when the vertebrae are the seat of new growths the bones thus attacked undergo rapid rarefactive change, they readily break or are crushed, and consequently the deformity and the compression-paraplegia resulting therefrom are often very sudden in onset.

*Other Local Conditions of the Spine.*—The spinal region at or about the seat of compression, when the source of mischief is extra-dural, is very commonly tender on pressure, whether applied directly, or indirectly in the axis of the body by pressing on the neck and shoulders. Furthermore, it is often hypersensitive, as shewn by the application of a hot sponge; and sometimes the skin is locally reddened from the paralysis of vasomotor fibres running in the nerve-roots which themselves are opposite the seat of disease or injury, and are implicated in the mischief. In diagnosis by physical examination great care must be exercised to distinguish between true local pain and the pains of mere neurasthenia (especially traumatic neurasthenia), which are spoken of as the hysterogenic points or zones of Charcot, and occupy certain well-known situations; the chief of these are the sixth and twelfth dorsal spines, the posterior iliac spines, and the coccygeo-sacral articulation.

In addition to the local signs just mentioned there is frequently the limitation of movement and fixation of the spine, due to pain causing the patient, voluntarily or involuntarily, to hold the spine in one position. This also must be carefully discriminated from the somewhat stiff attitude in which a traumatic neurasthenic patient often holds the dorso-lumbar region of his spine.

Finally, as regards local examination of the spinal column, it must be remembered that congenital absence or shortening of a spinous process is not infrequent, and has often been mistaken for a result of injury.

*Pain.*—The occurrence of pain in cases of pressure upon the cord

by new growths has been recognised from classical times; hence the name Paraplegia dolorosa, given to the cases of malignant disease of the vertebrae leading to paraplegia by compression of the cord. Though a striking and almost invariable accompaniment of tumour cases, pain is practically absent in other kinds of spinal compression. We will begin, therefore, with the pain of new growths. It is necessary to consider this pain from two points of view: namely, first, its character; secondly, its precise situation.

*Character and Mode of Production.*—The character of the pain in such cases is almost always burning and stabbing; this paroxysmal condition is not infrequently preceded, or accompanied, by steady aching which is only relieved at times by change of posture. This aching should be compared to that often observed in trauma. A very important feature is that the stabbing and burning pains are frequently called forth by movement, that is, by bending or rotatory twisting of the spine.

Pain of the kind just described is probably due to pressure on the sensitive dura mater and cord within it; but there is also a concurrent manifestation of pain produced by implication of the nerve-root. In these circumstances the pain begins in the pricking and stabbing manner, and then has a special character shooting along the distribution of the nerve whose root is directly pressed upon. However, such localised pain soon becomes merged in the diffuse pain due to pressure on the cord as a whole.

*Site of the Pain.*—Considering that every aid is required to establish a correct topographical diagnosis of the lesion, the importance of the fact that the pain is never referred to any part above the seat of the lesion is self-evident. This fact is doubly significant when the bifurcating character of the posterior-root fibres entering the cord is remembered, as also their association, each respectively, with reflex centres situated lower down the cord. If, of course, the lesion involve a nerve-root, the pain along which is a very definite feature, then this pain becomes of the utmost value in topographical diagnosis; but, unfortunately, as a rule, the pain is derived from the cord fibres, and then is referred to parts some distance below the lesion. Thus, in a case of compression of the lower part of the dorsal region the severe pains complained of were referred below the knees. Here I need only mention, as a warning, that in view of this fact that the localisation always tends to be too low, the occurrence of any apparently trivial pain must be carefully noted, and its distribution along the course of any given root accurately observed.

In the case of the general compression of the lower half of the spinal cord in pachymeningitis it is important to note that the site of reference of the pain is a generalised one parallel to the wide area of nerve-roots affected. Probably this affords the best means of differential diagnosis between pachymeningitis and tumour.

*The General Effect on Spinal Centres.*—The effect upon the spinal centres generally of compression of the spinal cord at some point above

them, is so to exaggerate their functional excitability as to produce overaction with resulting spasticity and exaggeration of reflex movements; but in very severe cases (for example, in traumatic severance of the cord) a loss of functional activity ensues (Bastian), the knee-jerks disappear, and in extreme cases remain absent, though in moderate ones they return (*vide* p. 244). Permanency of the loss of function suggests the existence of a diffuse traumatic myelitis.

The table (to face p. 575) shews the special representation of the various functions of the cord at the level of each segment; that is, at the level of each nerve-root.

**Ocular Symptoms.**—The nerve-fibres, excitation of which causes dilatation of the pupil, start from a centre in the floor of the posterior part of the iter, as yet not accurately localised. Such fibres run down in the lateral columns of the cord, and leave the latter by the second dorsal nerve-root to reach the inferior cervical ganglion of the sympathetic, and so pass up to the eye. This bundle of fibres is so well localised that, if at a focus in the cervical region compression be exerted with a little more strength on one side than on the other, the pupil of that side will be smaller. The very rare phenomenon of congestion of the disc in the same eye may occasionally be also observed; it resembles an early stage of optic neuritis.

**Cardiac Symptoms.**—Fibres which accelerate the heart run from a centre in the upper part of the floor of the fourth ventricle down the lateral columns of the cord, leave the cord by the dorsal nerve-roots from the fourth to the ninth, and reach the cardiac plexus by the sympathetic. These fibres, on careful examination, may be found functionally affected in compression of the spinal cord in the cervical and upper dorsal regions in one of two ways. Thus, they may be excited, this being the commoner; or they may be paralysed, as in acute compression of the cord. If the pressure be not very severe, and excitation occur, the pulse-rate will be found very high, that is, up to 140 per minute, without any corresponding constitutional condition to account for it. Very frequently this overaction on the part of these fibres is paroxysmal; the pulse-rate may rise rapidly, and after remaining up for a certain time fall again; and then, after an interval of some hours, may rise again, and so forth. In the paralytic state the heart-rate is slow, below the normal, the vagus being, apparently, no longer antagonised. It must also be noted whether the compression of the spinal cord affect the vasomotor channel, in which case it causes, as a rule, hyperaemia and oedema of the paralysed parts, or the so-called heat-fibres, that is, the thermotaxic, in which case the temperature may rise to 104° F. independently of any inflammatory mischief with which such pyrexia is usually associated.

**Respiratory Symptoms.**—The fibres conveying the innervation of respiratory movements must be divided into those supplied to the diaphragm and to the intercostal muscles respectively. Of these two groups the diaphragmatic is by far the most important, because the



intercostal muscles are more distant from the respiratory centre, as is evidenced by the fact that, when the compression of the cord is opposite some point above the fourth cervical nerve, the intercostal muscles may be completely paralysed while the diaphragm continues in full action. From this it is clear that the phrenic fibres in the cord are, practically speaking, more resistant (because possibly more numerous) than those for the intercostal muscles. "Deficiency" of the action of the intercostals is very commonly observed to result from compression of the cord as low as the second dorsal root, and is relatively quickly recovered from as soon as the source of the compression is removed.

The failure of respiration is not, of course, wholly one of affection of conducting channels alone; but this point cannot be further discussed here. The relative share taken by the bulbar and spinal portions of the central respiratory nerve mechanism, even in the case of the lower mammals, is itself an undecided matter.

**Vasomotor Symptoms.**—(a) *Constriction.*—The vaso-constrictor fibres probably leave the spinal cord, in man, at the levels indicated on the table opposite p. 575.

The conditions under which vaso-constrictor spasms appear to be maintained, or at any rate in which the calibre of the vessels is reduced, and in which vaso-dilatation does not occur, are seen in those cases in which there is long-standing compression of the cord, and in which atrophic changes have been set up in consequence of subacute degenerative changes. In these cases it will be observed that, besides the pallor and coldness of the paralysed parts, there are also evidences of narrowing of the vessels in the dry, harsh condition of the skin, coupled with which is often an accumulation of epithelium, producing a kind of exfoliative state of the epidermis, in patches and spots.

(b) *Vaso-dilatation.*—Whereas vaso-constriction is marked in a case running a slow course, vaso-dilatation is a sign of acute and severe compression of the cord. It shews itself in the paralysed limbs, causing swelling; and very commonly also in a pink flush. Sometimes the tumefaction of the tissues is practically limited to the synovial membrane of the chief joints of the limb; the knees or ankles, for example, the condition constituting the so-called arthritis observed in some cases of acute myelitis. It must not, of course, be confused with the acute synovitis of a pyaemic nature, which occasionally arises in connexion with the bed-sores of acute myelitis, and which goes on to suppuration—a stage which the congestive synovitis of vaso-dilator origin never reaches.

**Visceral Symptoms.**—The abdominal viscera, whose innervation is disturbed by compression lesions of the spinal cord, are chiefly the alimentary canal and bladder.

*Alimentary Canal.*—In extensive crushing lesions of the cord, with probable intra-medullary haemorrhage, causing compression if not destruction of the centres from which the fibres passing into the splanchnics take origin, the small intestine is sometimes paralysed.



(a) *Intestine*.—In these circumstances meteorism is produced, the abdomen is notably distended, and, though there is no acute pain connected therewith, the patient nevertheless very often has severe discomfort, or curious sensations of oppression connected with the dilated condition of the parietic gut; especially a sense of peristaltic movements involving successive segments down to a certain point where they stop, suggesting a block. In the large intestine the expulsive force is very greatly diminished; but the bowel can be caused to contract by suitable local stimulation, as by the faradic current, or by injection of castor oil or turpentine. In extensive lesions of the sacral-root portion of the lumbar enlargement the sphincter ani may be completely paralysed.

(b) *Bladder*.—The chief site of the representation of this important viscus in the lumbar enlargement is opposite to the second sacral root. And in all conditions of compression of the cord every possible variety of interference with the action of the organ may be observed as follows:—  
(i.) In an early spastic stage there may be retention due to tonic spasm of the sphincter vesicae. (ii.) In all forms of gradual compression there is diminished holding power of the sphincter; as the paresis increases, this becomes a complete loss of control, and then the flow is incessant or occurs at brief intervals. As an intermediate grade what is called the overflow condition is sometimes observed.

(c) *Secretory Glands*.—A clinical condition, comparatively speaking overlooked, and yet one of considerable value for the purposes of diagnosis, is the condition of the secretory glands and notably of the sweat-glands in the skin of the paralysed parts, which are found, in an early stage, to exhibit paralytic hypersecretion; in the later stage there is failure of the normal function.

(i.) *Sweat Glands*.—Strauss employed pilocarpine in facial paralysis to test the loss of function of the secretory fibres of the seventh nerve. It occurred to me that this method could be employed to map out in like manner the area of skin below a compression lesion of the cord by comparing its condition with that of the skin above the lesion, and thus obtaining a line of demarcation. In the majority of cases the injection of a quarter of a grain of pilocarpine will produce a sharp contrast between the two areas, the line of junction being marked by a line of drops of sweat. With such a test, of course, care must be taken that there is no tendency to bronchorrhoea, a matter of special importance in cases of fracture in the cervical and cervico-dorsal regions when the intercostal muscles may be thrown out of gear.

(ii.) *Other Glands* (kidneys, mucous glands, etc.)—The secretory activity of the kidneys may be diminished by lesions in the lumbo-sacral region (see topographical table, to face p. 575), and this diminution aids in estimating the degree of loss of function and injury due to the lesion. Similarly the mucous glands of the bowel sometimes exhibit hypersecretory activity.

**Trophic Changes**.—This is not the place to enter into a discussion of the mechanism by which trophic neuroses are set up (p. 79), but it is

necessary to recite shortly the alterations produced by compression of the cord. In the first place, there is the great difference between the trophoneuroses produced by an extra-medullary or intra-medullary lesion, or by a very circumscribed or by a general lesion, respectively. For example, a restricted extra-medullary lesion will hardly cause a bed-sore, and will lead but very gradually to inflammatory conditions in the skin where it is pressed upon, and most likely in proportion as the lesion invades the functional activity of the cord. It is quite otherwise in an intra-medullary lesion, or in a very extensive extra-medullary compression of a large portion of the cord; in such instances, unless the nurse be vigilant, bed-sores are rapidly formed; the skin, after being reddened for perhaps two or three days, becomes oedematous, and soon the centre of the red oedematous area is found to be necrotic, an eschar being formed, the depth of which may reach to the nearest bony surface. Such trophic changes are not confined to the parts pressed upon as the patient lies on the bed—for instance to the sacral region, or the heels—but may occur wherever the skin surfaces are in contact. Relief of the pressure on the cord by laminectomy always stops this kind of mischief, and brings about the healing of sores. Unless the mechanical pressure be re-established there is no relapse. It is plain, therefore, that wherever these trophic lesions are pronounced, active and serious pressure may be inferred. In long-standing cases of severe compression-paraplegia the skin of the paralysed parts becomes harder, the epithelium tends to desquamate, and, as there is little or no normal secretion from the sweat or sebaceous glands, the surface is harsh and dry. There is seldom any glossy skin such as is seen in disease or injury of the peripheral nerves (*vide* p. 82).

**Site of the Lesion.**—The very important problem of the precise seat of the mischief in the cord must be considered under the following headings: (i.) Determination of the level of the lesion in the cord. (ii.) Determination of the corresponding point on the exterior of the body. (iii.) Determination of the nature of the lesion. Of these headings the last rests entirely on the facts of pathology, to works on which subject reference is made; there remain, therefore, for notice Nos. (i.) and (ii.)

(i.) *Determination of the Level of the Lesion in the Cord.*—The site of a lesion in the cord must be determined by observing the disturbance it effects in the functions of the following parts: (a) of the conducting channels from encephalon to nerve-roots; and reversely (b) of the nerve-centres.

(a) 1) *Conducting Motor Channels.*—The exact seat of a complete transverse lesion of the cord can be estimated by observation of the highest of the muscles, innervated from points below the lesion, that are visibly thrown into action by voluntary effort. Unfortunately, whereas this is easy of analysis when the muscles in question are those of the limbs, it is difficult to be sure when an intercostal muscle or a single segment of the rectus abdominis or erector spinae is concerned; here in

a great measure the whole mass seems to move, although only certain portions are really in action.

The seat of an incomplete lesion must be ascertained by reference to the table (to face p. 575), wherein the local innervation of the respective muscles and groups of muscles which are paralysed can be ascertained.

(a 2) The Conducting Sensory Channels.—As in the case of interference with the outgoing channels of conduction from the encephalon, so the lowest possible border of aesthesia that can be marked is taken as the chief means of determining the segment involved; but here we have to discriminate carefully between the precise edge of the area of absolute loss of sensation, due to pressure on the conducting channels, from the zone of paraesthesia, or often of hyperaesthesia, due to the local implication of nerve-roots immediately above the anaesthetic area (*vide infra*). The topographical outline of the various nerve-root zone areas are shewn in Figs. 71, 72, 73, 74, a scheme which certainly seems to be more in accordance with clinical data than the other well-known schemes that have been published. They are to be similarly applied in determining the position of incomplete lesions.

The foregoing applies to the tactile sense and to the temperature sense, which channels run partly in the posterior and lateral columns of the cord, and in the grey matter, the two latter including the internuncial and collateral fibres.

To the channels mentioned above must be added the direct cerebellar tract and the antero-lateral tract, which probably subserve equilibrial and "muscular sense" functions.

(a 3) The Channels for Conduction of Pain.—The existence of analgesia produced by compression of the channels of conduction of painful impressions is a most important symptom; because, since the original experimental discoveries of Schiff and the subsequent clinical researches into the pathology of syringomyelia, there seems to be little doubt but that the channels for the transmission of painful impressions lie in the grey matter of the cord near the central canal. Consequently the presence of analgesia signifies, as a rule, the existence of a lesion (that is, myelitic or haemorrhagic) greatly affecting the viability and recuperability of the central mass of the spinal cord. As regards exact localisation, since these channels are internuncial in character, it follows that, excepting where a complete transverse lesion of the cord occurs, the determination of the border of analgesia will always be less definite than that of the areas of other affections of the senses.

(b) Nerve Centres.—Of course discrimination must be made in every case between the amount of failure due to the disorganisation of a centre and that caused by interruption of a channel of connexion with the encephalon. Systematic localisation of a lesion causing disorder of the various central mechanisms of the cord may be arranged advantageously by exploring the following functions in the order given:—Systemic muscles; motion. Systemic surfaces; sensation. Sensation. Reflexes; superficial, deep. Orbital, that is, intraocular, movements. Cardiac



movements. Respiratory movements. Vasomotor movements; constriction, dilatation. Innervation of the alimentary and renal viscera. Innervation of the secretory glands. Trophic changes.

The details must in each case be worked out by the table facing p. 575.

(ii.) *The Determination of the Corresponding Point on the Exterior of the Body.*—The correspondence between definite points in the cord and the bony prominences of the spine and surface-markings is stated on the table; but there are a few points worthy of mention.

Thus, the fixing of the vertebra prominens is sometimes difficult; but the spot can be made out in a stout subject as the first spine felt on drawing the finger firmly down the ligamentum nuchae. In a thin person, in whom confusion may arise from the number of palpable spines, the 7th cervical can be distinguished, as a single knob, from the bifid 6th cervical.

The 3rd cervical arch is commonly quite concealed under the laminae of the 2nd vertebra.

The 12th dorsal can often be made out more correctly by tracing up the last rib to the spine than by counting down from the 1st dorsal.

The 3rd lumbar can be estimated correctly by drawing a horizontal line at the level of the iliac crests.

**Skiagraphy.**—The relation of the lesion to the exact level of the cord affected by the pressure can be largely determined by skiagraphy. No case should be regarded as completely examined without the aid of a skiagram. Further, the shadow of a tuberculous lesion, the indefinite edge of a sarcoma, and so forth, are data on which absolute reliance can be placed, and therefore skiagraphy affords invaluable evidence of the nature as well as the position of the mischief.

**Treatment.**—*Treatment of Caries of the Spine.*—Caries of the spine is a very different disease in the young child, in persons of early adult age, and in those of advanced age, respectively. It may safely be said that in the first case adequate rest and extension will, in the majority of instances, cure the disease; that in the last class the condition is an exceedingly intractable one whatever is done; and in the middle group that the most active and early steps are necessary to obtain a satisfactory result. The next point to be determined in any given case is the presence or absence of an abscess,—to determine, in short, whether the compression of the spinal cord be due to the bony deformity, or to the pressure of an abscess sac. In the latter condition operation becomes an immediate necessity, whereas in the former it should be resorted to after other measures have failed.

The diagnosis of the presence of an abscess, simple enough when the seat of mischief is the lamina of a vertebra, is by no means easy when the disease is in its common position, that is, in the bodies of the vertebrae. We may note that, as stated above, the coexistence of pyrexia (often very slight), with increased spasticity and contracture of the paralysed limbs, forms the best foundation for the suspicion of an



abscess. When the abscess has been exposed by laminectomy, it must be opened by the side of the theca, thoroughly scraped out with a sharp spoon, disinfected with strong 1 in 500 perchloride solution, and the cavity drained and dressed assiduously, so as to obtain obliteration of the sac. In this connexion the difficulty of determining when the compression of the spinal cord is thoroughly relieved must again be called to mind; for in some instances it is necessary to repeat the scraping out and disinfection several times before the tuberculous mischief is arrested and restoration of the cord established.

To adopt a rough general rule for the influence of age the following is justifiable:—Any case seen at its very beginning should be treated by extension of the spine, with a modification of the apparatus in which the head and arm-pits are fixed by suitable straps and bands to elastic accumulators, the other ends of which are attached to the wall; and then counter-extension, of a similar kind, is to be provided by laced-up anklets to which rubber accumulators, fastened to the end of the bed, can be attached. The duration of such extension varies, of course, according to the signs of improvement, which ought to begin to appear within two months. If in the young adult a favourable change is not noted at the end of this period a laminectomy should be performed. In persons of advanced age operation affords the only possible assistance. It is rare that in the young adult any treatment is very serviceable, unless it be laminectomy in an early stage of the disease. A certain proportion of cases, however, those that bear extension well, can be cured by such treatment.

In strong contrast with such cases are those of persons suffering from senile tuberculosis, in whom the disease tends to progress rapidly, and to attack, not the bones only, but also the theca; leading to a very definite myelitic softening of the cord. If the patient's condition renders it possible, a complete laminectomy ought to be performed.

In connexion with this general subject of treatment of caries producing compression of the spinal cord, attention must be paid to other points than those which have been referred to under the heading of motor and sensory paralysis; these are body weight, and condition of the parietic parts (for example, swollen or red suggesting vasomotor paralysis). If there be any such symptoms the inference follows that the spinal cord is already beyond the possibility of amelioration, and in a condition of diffuse myelitis.

*Treatment of Deformity of the Spine due to Caries.*—Recently the old and somewhat barbarous treatment of the kyphosis due to caries by immediate reduction has been revived, and often improperly regarded as treatment of caries. It is very questionable if any mechanical advantage accrues to the patient from straightening out the curve.

*On the Treatment of New Growths compressing the Spinal Cord.*—*Intra-dural and Extra-medullary.*—As soon as a local lesion is diagnosed, and the assumption that it is a neoplasm sufficiently justified, then laminectomy should be performed, care being taken that the part of the cord exposed

corresponds with the highest nerve-root whose function can be found in any degree altered, even in the slightest. When the tumour is shelled out the bleeding is to be stopped; this can be easily done with a little gentle pressure, or by taking up any obstinately oozing vessel with a very fine needle and horse-hair ligature.

*Intra-medullary.*—These are sometimes met with in cases in which an exploratory operation has been performed, cases in which it was not possible to diagnose the seat of the growth correctly; but, as a rule, it is very difficult to detect their presence in the intact cord. Further, it is impossible in the present state of surgery to remove them without some slight injury to the remainder of the cord.

*Extra-dural.*—In cases of extra-dural sarcoma of the spine operative interference to preserve life is, of course, useless; but it may be undertaken, if necessary, to relieve extreme pain, which can easily be done as the latter is produced purely mechanically. Cases of primary sarcoma considered inoperable may with advantage be treated with injection of Coley's fluid, and local necrosis thus induced, with consequent relief of the pressure.

*Treatment of Trauma.*—(a) *Immediate Reduction.*—A moderate degree of fracture-dislocation of the spine, with consequent compression of the cord, has in some cases been treated fairly successfully by immediate reduction under an anaesthetic, and fixation of the spine with suitable plaster of Paris or other apparatus.

(b) *Operative Treatment.*—In the majority of cases fracture-dislocation of the spine produces such severe compression of the cord as to make the symptoms during the first few days very urgent, and the condition of the patient a perilous one. In this condition of affairs it is better to postpone any active interference for a few days until the immediate effect of the shock has passed off, and then to do a laminectomy. The object of the operation is not so much to deal with blood extravasated into the neural canal, which, as stated before, is rarely present in such quantity as to cause compression symptoms, but to remove fractured laminae, or projecting portions of the vertebral bodies, or, not infrequently, intervertebral discs, which are the most frequent means of compression. Contusion of the cord, with resulting haematomyelia, cannot be satisfactorily dealt with, as the extravasation is diffused through the substance of the cord (art. "Haematomyelia," p. 680).

*Treatment of Pachymeningitis.*—Pachymeningitis can only be treated by laminectomy, but the operative release of the pressure appears to have but little benefit if the patient has attained an age of forty-five to fifty years.

VICTOR HORSLEY.

## DISEASES OF THE SPINAL MENINGES

By J. S. RISIEN RUSSELL, M.D., F.R.C.P.

THE most important morbid conditions of the spinal meninges are the following:—

I. Vascular disturbances:—1. Hyperaemia. 2. Haemorrhage.

II. Inflammations:—1. External pachymeningitis. 2. Internal (haemorrhagic) pachymeningitis. 3. Cervical hypertrophic pachymeningitis. 4. Syphilitic meningo-myelitis (*vide* p. 726). 5. Leptomeningitis: (a) Acute simple; (b) Cerebrospinal; (c) Tuberculous; (d) Chronic leptomeningitis; (e) Scrous spinal meningitis.

III. Tumours of the meninges (*vide* p. 868).

The following morbid states are only of pathological interest, as they do not give rise to any clinical manifestations by which they can be recognised, or which call for treatment.

IV. Calcification of the dura and arachnoid.

V. Pigmentation of the arachnoid.

VI. Hydrorrhachis.

VII. Varicosity of the veins of the pia mater.

I. VASCULAR DISTURBANCES.—1. **Hyperaemia of the Spinal Meninges.**—It is common on necropsy to find hyperaemia of the spinal meninges, the vessels being so engorged as to suggest a pathological process, but in the majority of instances the condition is due to the fact that the cadaver is placed on its back, so that gravity determines the flow of blood into the dependent vessels of the spinal meninges, a state of things no doubt accentuated by the long time that many of these patients have been lying on their backs during a protracted illness. In addition to the engorgement of the vessels there may be a diffuse redness consequent on decomposition of the blood, with diffusion of its colouring matter. It may be very difficult, therefore, to determine that the hyperaemia has any other significance, even where the clinical manifestations had led us to expect changes of the kind; and to detect anaemia of the meninges, even if this had existed during life, may be impossible. Much error has resulted from attempts to formulate a group of symptoms by which hyperaemia manifests itself clinically, and by the supposition that the diagnosis has been borne out by the morbid changes met with after death; whereas in reality the changes to which so much importance has been attached have been none other than those occasioned by gravity and by decomposition.

Diseases attended by convulsions during life shew distinct hyperaemia of the spinal meninges after death, as a consequence of disturbance of the respiration and circulation, especially in tetanus, eclampsia, dentition-



convulsions, and chorea. Poisons which induce convulsions or asphyxia, such as strychnine, prussic acid, and carbonic acid, are attended with a like result.

In the early stage of a meningitis, if death have resulted before the stage of exudation, we may find no more than an intense congestion of the meninges, which are of a rosy hue, the vessels being dilated and engorged; and, what is of great importance in establishing the pathological significance of the changes, the presence of minute hæmorrhages which may often be detected if carefully looked for.

Whether hyperæmia of the meninges may exist apart from the above conditions is difficult to decide. Those who hold that such is the case assign as its causes accidents and other conditions attended with pain in the back and lower extremities, and regard tremors, weakness amounting, it may be, to actual paralysis, and spasms as further symptoms. Suppression of the menses or of a hæmorrhoidal flux, chronic uterine and abdominal diseases, and pregnancy have also been held responsible for the condition. Prominent among those who have upheld the view that congestion of the spinal meninges is a definite process are Frank and Ollivier. The clinical picture of the condition, as represented by the latter observer, resembles the course of Landry's paralysis; for the onset is attended with weakness of the lower extremities, the loss of power spreads upwards until the upper part of the trunk is reached, and it is accompanied by painful subjective sensations of pins and needles, and the like. There is then a stationary period during which the pulse and respirations remain slowed, and the paralysis incomplete; and this may be followed by complete disappearance of all symptoms in the reverse order to that of their advance. He includes cases of suppression of the menses, chills, abdominal affections, and so forth—in which there is pain in the spine radiating to other parts and accompanied by incomplete paralysis. The variations and irregularity of the course, together with the rapid recovery in some of the cases, are explained by the variations in the amount of blood contained by the meninges. Ollivier further adduces, in support of his contention, that on necropsy in these cases hyperæmia of the spinal meninges is found, whilst the spinal cord itself is intact.

Plausible and even justifiable as these arguments may seem, we shall hesitate to attribute cases in which the symptoms are at all severe to a mere congestion of the spinal meninges; and cases in which such symptoms exist during life, and in which, nevertheless, congestion of the meninges alone is found after death, without any evidence of implication of the spinal cord itself, appear to belong rather to the category of spinal cord affections in which toxic influences disturb nerve function, and perhaps arrest it, without producing lesions capable of detection by methods hitherto in use. We do not know of any group of symptoms indicative of congestion of the spinal meninges to the exclusion of any other affection. Nevertheless, when we meet with pain in the back, radiating it may be to the lower extremities which are weak, in association with suppression of the menses or of a hæmorrhoidal flux, it is not unreasonable to assume that



the symptoms may be due to congestion of the spinal meninges, and the same may be said of cases in which backward pressure in the circulation exists. Similarly in the course of fevers, when pain in the back and weakness of the lower extremities are present, as is especially apt to occur in small-pox and enteric fever, a like explanation seems reasonable, although the action of toxins on the nerve elements cannot be excluded.

When variations in the intensity of the symptoms are rapid and transitory, it is reasonable to assume that they may be due to hyperaemia; and, according to Brown-Séquard, the most certain sign of congestion of the spinal meninges is a greater paresis in the morning than in the evening in patients who are up during the day.

**2. Haemorrhages into the Spinal Meninges.**—(Haematorrhachis; Meningeal Apoplexy.)—In this condition blood is found extravasated either between the dura mater and bone of the walls of the neural canal (extra-meningeal haemorrhage), or within the dura mater (intra-meningeal haemorrhage). In the latter case the blood either exists in the arachnoid cavity between the dura and arachnoid (subdural haemorrhage), or between the arachnoid and pia mater (subarachnoid haemorrhage).

*Causation.* (i.) *Extra-meningeal Haemorrhage.*—This is the most common form, and is usually the result of some trauma in which the spinal column is injured, and in which the dura mater participates; or in which there is simply shock. Another rare cause of extravasation of blood in this situation is the rupture of an aneurysm into the spinal canal; and in operations on the spinal column blood-clot may, of course, be found lying on the dura. Tetanus and any of the conditions which induce spinal congestion may be attended by such haemorrhages; among these may be mentioned more especially various intoxications, eclampsia, trismus neonatorum, dentition-spasms, and the like. In diseases of the heart or lungs, in which there is backward pressure in the portal system, haemorrhages may also occur. I have seen a considerable amount of fresh clot outside the dura, in the lower cervical and upper thoracic regions, in connexion with a purulent external meningitis.

(ii.) *Intra-meningeal haemorrhage* is almost as common as the extradural variety. In these cases the blood may either be derived locally from rupture of veins in this situation, or it may find its way into the arachnoid sac from elsewhere, usually from the intracranial cavity. When of local origin, the cause may be an injury which has resulted in fracture of the spinal column, with tearing of the dura, or rupture of the vessels of the pia, with or without laceration of the spinal cord. It is, however, well to remember that, without fracture of the spine, blows on the back, or falls on the buttock or feet, may give rise to meningeal haemorrhage. Spontaneous non-traumatic haemorrhage is very rare and its mode of origin uncertain; probably some of the cases are due to strain: but whether any are to be accounted for by arrested menstrual or haemorrhoidal flux is doubtful. This accident may happen to children

at the time of birth, either when forceps are used to aid delivery, or, more commonly, in cases of extraction by the feet, when there is separation of a vertebra at the epiphysial line with rupture of the anterior vertebral ligament. Ruge met with this condition in 8 out of 64 cases of the latter mode of delivery. Spinal meningeal haemorrhage, however, may occur apart from luxation of the spinal column; Litzmann found such haemorrhage in 33 cases out of 81 in necropsies on new-born children; but in 23 of the cases the blood was wholly extra-dural. In operations on the spinal cord, or on the nerve-roots, necessitating opening of the dura mater, blood may be found extravasated in this situation. As in the case of extra-meningeal haemorrhage, so here the haemorrhage may be met with in cases of death from convulsive affections, such as tetanus, puerperal eclampsia, epilepsy, and strychnine poisoning.

In the infective fevers small haemorrhages are not uncommon: notably in haemorrhagic small-pox; and in diseases with a general tendency to haemorrhage, such as scurvy, small haemorrhages occur; they may be plentiful in meningitis when death results before the stage of pus formation is reached; or a large collection of blood may be met with in association with purulent meningitis.

Instead of originating locally, the blood may find its way into the neural canal from elsewhere; the largest of such haemorrhages result from rupture of an aneurysm of the basilar or vertebral artery at the base of the brain. In operations on the posterior fossa of the skull, necessitating opening of the dura mater, blood may escape into the spinal meninges; but the amount is never sufficient to be of any serious moment. A cerebral haemorrhage which bursts into the lateral ventricles may find its way to the spinal meninges; or the haemorrhage may be derived from the base of the brain as the result of an injury. In cerebral apoplexy of the new-born, the result of difficult labour, the blood may find its way into the spinal canal; in the cases in which Litzmann found haemorrhage in the spinal arachnoid cavity he found also haemorrhage in the intracranial cavity, mostly meningeal blood extravasations.

*Morbid Anatomy.*—Owing to the usual position of the cadaver on the back, the veins outside the dura mater become greatly distended; and when they are divided, as the neural canal is opened, a good deal of blood may escape. A haemorrhage of ante-mortem origin may thus be looked upon as merely of this accidental character; but more commonly the error consists in regarding the post-mortem condition as of ante-mortem origin.

In the extra-dural variety of haemorrhage the blood is usually clotted and not large in amount; it is derived from the plexus of veins between the dura and the bone, and the blood escapes into the loose cellular tissue in this situation. Partly because the space between the dura and bone is larger dorsally than ventrally, and partly because of gravitation, the blood tends to remain more or less confined to the dorsal aspect; but where the haemorrhage is more extensive, the blood-clot

may be found extending along the nerves through the intervertebral foramina. It is rare, however, to meet with an extravasation sufficiently large to give the dura a compressed or flattened appearance; though the soaking of the membrane in blood may result in staining which is obvious on looking at its inner surface.

When the haemorrhage is intra-meningeal it may be small in amount, or it may fill the greater part of the subdural sac; when beneath the arachnoid it may, similarly, be limited to a few segments of the spinal cord, or it may extend throughout the greater part of the length of this structure. In the subarachnoid variety the blood is usually derived from vessels of the pia mater; and when thus local in origin the haemorrhages are rarely large, but they may be so when the blood gravitates to the spinal from the cerebral meninges. The reverse of this may obtain, as in a case recorded by Leprestre, in which a spinal haemorrhage into the arachnoid cavity not only reached the pons but also burst through the valve of Vieussens, and reached the lateral ventricles of the brain. On the other hand, independent haemorrhages may arise in the intracranial cavity and neural canal as the result of a common cause. The spinal fluid is frequently blood-stained, as Colugno also observed in new-born children dead of asphyxia. When the haemorrhage is subarachnoid in situation the spinal cord is especially liable to damage; and, apart from this, the various levels of the cord may be compressed in variable degrees.

*Symptoms.*—It is impossible to formulate any distinctive symptomatology for extra-dural haemorrhages. Where they result from an injury it is not possible to distinguish the symptoms consequent on the haemorrhage from those directly due to the injury; and it is exceedingly rare to meet with an extra-dural haemorrhage large enough to produce symptoms of compression of the spinal cord. Such a result may, however, come about through rupture of an aortic aneurysm into the neural canal.

The smaller multiple haemorrhages, whether extra- or intra-meningeal, as a rule do not cause any symptoms; and symptoms may be absent or ill-defined even where the intra-meningeal haemorrhages are larger; or symptoms, if present, may be masked by those of the disease in the course of which the haemorrhages had occurred. So also when intracranial haemorrhage coexists with that into the spinal meninges the symptoms due to the former condition may completely overshadow those of the spinal affection; or death may approach so rapidly that the spinal symptoms have not time to appear.

When symptoms of meningeal haemorrhage do exist they are almost the same in extra-meningeal and intra-meningeal cases; and, in the absence of any serious concomitant lesion of the spinal cord, irritative phenomena preponderate over the paralytic.

*Pain.*—Sudden and severe pain in the back is usually the first, and is certainly one of the most frequent signs of the condition; its position corresponds to that of the haemorrhage, and, as the cervical region of the cord is most commonly the seat of such extravasations, it is



frequently felt between the shoulders and in the neck; but it may also be spread out over the greater part of the length of the spinal column, and is often severe in the loins. This pain is not increased by pressure on the spinous processes of the vertebrae, although it is made worse by movement of the patient, such as turning round and sitting up.

In addition to the pain in the back there are usually paroxysmal attacks of lancinating pain along the course of the nerve-roots which pass through the meninges at the seat of extravasation, and are irritated by the clotted blood. These pains are generally very severe, and may be burning or darting in character, and accompanied by various paraesthesias, such as feelings like pins and needles, tingling and the like, referred to the parts affected by the pain, and felt in the intervals between the paroxysms. The distribution of these sensory phenomena depends on the seat of the haemorrhage: when in the cervical region they are referred to the neck and upper extremities; when in the thoracic region, girdle pain appears; and when the meninges of the lower part of the cord are affected the lower limbs are the seat of these abnormal sensations.

*Hyperaesthesia and Hyperalgesia.*—Pressure on the skin or muscles causes a varying degree of discomfort, which may amount to actual pain; this is most common in the lower extremities. Erections may be attended with pain, as may the passage of urine and faeces.

*Anaesthesia* may exist over a wide area in association with hyperaesthesia, but it subsequently becomes much more restricted. Such residual anaesthesia is especially prone to involve the perineum, the genital organs, the bladder, and the rectum.

*Muscular Spasm.*—This may give rise to stiffness of the back; a condition which may be due also to voluntary contraction of the back muscles to prevent the pain of movement. The spasms are probably reflex in origin, and may be so severe in the back as to cause opisthotonos. Rigidity and active jerkings are more frequently met with in the lower than in the upper limbs. Sometimes, however, the convulsive movements are general, whereas in other cases certain muscles are in persistent contraction.

*Motor Paralysis.*—True loss of motor power, which is commonly met with in the lower limbs, must be distinguished carefully from abstention from movement on account of pain. It is not common for the loss of power to be complete, though it occurs in some cases. When power is lost at the onset it means either that the cord is compressed by a large extravasation of blood, such as may result from the rupture of an aneurysm, or that there has been haemorrhage into the cord as well as into the meninges. When the cervical meninges are the seat of the haemorrhage, a diplegia brachialis may result.

*Tendon-jerks.*—These are absent in the lower limbs at the onset, and remain so when the lesion is in the lumbar region; but when the meninges of the thoracic cord are involved the tendon-jerks may be preserved.

*Sphincters.*—Retention of urine is frequent; incontinence also occurs,



though more rarely. Priapism is especially frequent at the outset, and is more common when the haemorrhage is in the cervical region.

Such are the symptoms that indicate an affection of the spinal meninges which is interfering with the functions of the spinal cord and of its afferent and efferent nerve-roots. The precise grouping of the symptoms in a given case will, of course, depend on the seat of the lesion. Thus, when the meninges of the cervical region of the cord are affected, the pain and rigidity are in the neck and arms; parietic symptoms may be present in the latter as well as in the legs; respiration may be interfered with; there may be difficulty of swallowing, and one or both pupils may become dilated. Girdle pain, with a varying degree of paraplegia and, usually, with preservation of the reflexes, characterises a lesion of the thoracic cord; and when the lumbar region is concerned, the pain is referred to the legs, in which signs of loss of motor power come on early, with absence of the tendon-jerks, and paralysis of the sphincters allowing incontinence of urine and faeces. Cerebral symptoms are absent as a rule; when present they are usually due to a simultaneous intracranial lesion, either independent of the spinal haemorrhage, or giving rise to escape of blood from the intracranial cavity into the neural canal. Or again, a haemorrhage, primarily spinal, may find its way into the intracranial cavity, and thus give rise to cerebral symptoms. Apart from this, however, consciousness may be lost for a short time, owing probably to shock; and delirium and even coma have been observed.

In turning to consider the signs of haemorrhage as opposed to any other lesion of the spinal meninges, the sudden apoplectic mode of onset is of primary importance. Not only is the onset sudden, but the maximum effect of the lesion is rapidly reached—in two or three hours as a rule; though sometimes a day or two may intervene. In very exceptional cases, however, instead of this sudden onset with rapidly increasing intensity of symptoms up to the maximum there is a gradual mode of onset in which there is no pain, and in which paralytic phenomena are developed slowly.

When, moreover, there is a history of an injury capable of inducing a meningeal apoplexy, the probability of haemorrhage is of course strengthened.

The course of these cases varies according to the amount of haemorrhage, its seat, the degree of concomitant damage to the spinal cord, and the presence or absence of complications, due on the one hand to a simultaneous cerebral lesion, and on the other to secondary effects of the spinal lesion, such as bed-sores and cystitis.

The usual course in favourable cases, after the maximum primary effect of the lesion is reached, is a diminution of the symptoms for the next few days, to be followed by an increase during the period of inflammatory reaction. This exacerbation usually takes place between the second and the fourth day. The amount of increase of symptoms at this time and their duration vary; there may be some pyrexia, and death may ensue; but more commonly, after lasting not more than a fortnight,

permanent improvement sets in, absorption of the blood-clot takes place, and in the course of four to six weeks the symptoms may yield or even disappear, provided that proper rest and therapeutic measures have been enforced.

Yet such a favourable course may be interrupted by severe meningitis, by the occurrence of acute bed-sores or cystitis. Where there has been concomitant injury to the cord, the meningeal symptoms disappear only to leave the phenomena due to a lesion of the cord more prominently in relief, whether that lesion be purely traumatic, or aggravated by secondary myelitis. The most common indications of the implication of the spinal cord itself are marked paralyses, especially of the sphincters, during the time that the meningeal symptoms are prominent, and the persistence of paralytic phenomena, accompanied it may be by muscular atrophy, after the more characteristically meningeal symptoms have passed off. But it is always a matter of great difficulty to ascertain how much of the clinical picture may be accounted for by the meningeal haemorrhage alone, and how much ought rather to be attributed to concomitant injury of the cord; this question will be considered more in detail when we discuss the diagnosis of meningeal haemorrhage.

Death occurs most commonly a few hours after the onset of the symptoms, and may be due to shock or exhaustion from the intense pain; on the other hand it may be due to respiratory difficulties consequent on the combined effects of paralysis and spasm; or blood may find its way into the intracranial cavity and thus cause death; or this result may be brought about by a simultaneous haemorrhage in the intracranial cavity. Indeed, in the last contingency, the intracranial lesion may be so severe as to cause death before symptoms of the spinal lesion have had time to make themselves manifest.

*Diagnosis.*—Lumbar puncture affords a ready means of diagnosis, but the possible risk of infection must not be forgotten. Apart from this, the most important indications on which a diagnosis may be based are the sudden onset of symptoms; especially pain in the back, which may be so violent as to cause the patient to cry out; and the signs of meningeal or nerve-root irritation predominating over any paralytic symptoms present. In the very exceptional cases in which the onset of symptoms is gradual and without pain, it is impossible to arrive at a certain diagnosis. When an injury precedes the sudden appearance of the above symptoms, diagnosis is made considerably easier in so far as the question of haemorrhage is concerned; but not necessarily so as regards a discrimination between extravasation limited to the meninges and concomitant haematomyelia. Severe paralysis of motion and of the sphincters always indicates a simultaneous lesion of the spinal cord; moreover, such paralytic symptoms are present from the outset, and, even if not pronounced at first, rapidly become so. In uncomplicated meningeal haemorrhage, on the other hand, irritative phenomena precede paresis. In attempting to distinguish an uncomplicated case of haematomyelia from one of haematorrhachis, we have to rely on the fact that in

the former condition paralytic phenomena predominate over those due to irritation of the meninges and nerve-roots. Pain in the spine is more commonly absent in haematomyelia than in meningeal haemorrhage, and when present is more localised and does not tend to radiate. In patients who recover, a residuum of paralysis is usually left; together with, it may be, some muscular atrophy, some affection of sensibility, interference with the sphincters, or other indication of structural damage to the spinal cord itself.

We have seen that meningitis may result as a secondary effect of a meningeal haemorrhage; but, apart from this, the inflammatory affection may be distinguished from a spinal apoplexy by the gradual onset of the symptoms and the presence of pyrexia from the beginning. The absence of pain, and of signs of irritation of the meninges and nerve-roots, together with the presence of well-marked paralytic phenomena, serve to distinguish a myelitis.

*Prognosis.*—Much depends on the exact time when the patient is seen and the probable seat of the haemorrhage; extravasation in the cervical region being especially grave, owing to interference with respiration. Death may result at the onset, or soon after; but the prognosis improves when the maximum effects of the haemorrhage seem to have been reached. The initial danger past, there are still grounds for fear until the inflammatory stage is over; after four to six days, however, without evidence of meningitis, the prognosis, so far as life is concerned, becomes very good.

As regards recovery otherwise, meningeal apoplexy, in common with haemorrhages in general, is relatively curable; but the degree of recovery to be expected largely depends on the effect upon the spinal cord. In the absence of much damage complete cure may result, and this with a degree of rapidity depending on the severity of the initial lesion, and on the contingency of bed-sores or cystitis; or there may be some residuum in the form of sensory defects, slight paralysis, weakness of the sphincters, or, perhaps, muscular atrophy; yet under proper treatment even these may be recovered from in the end. It is needless to say that the presence of a simultaneous lesion of the spinal cord very greatly reduces the chances of complete recovery.

*Treatment.*—Absolute rest and careful nursing are all-important in the treatment of meningeal haemorrhage; and it is equally important to attend to the posture of the patient. Even passive movements are best avoided in these cases as much as possible; and the patient ought not to lie on his back, but should be carefully propped in position on one or other side by means of cushions or bolsters; moreover, a few hours should be spent in the prone position every day. Indeed, many such patients are unable to lie on their backs on account of the increase of pain which this posture occasions, and there can be little question that a supine position may aggravate the damage.

Some observers recommend venesection in robust subjects, in order to lower blood-pressure, and thus to facilitate the arrest of haemorrhage.



When this procedure is not thought advisable, local blood-letting may be tried, by means of wet-cupping or leeches applied over the supposed seat of hæmorrhage; or the leeches may be applied to the anus. In feeble persons in whom even these measures are best avoided, dry-cupping over the supposed seat of the hæmorrhage is sometimes tried. In any case ice should be applied to this part of the spine, and salts of calcium or ergotin may be administered. In order to relieve the violent pain, and to keep the patient as quiet as possible, morphine should be given subcutaneously, or some other anodyne substituted. In the next place free action of the bowels must be secured.

Where there is reason to suppose that the spinal cord is being compressed by blood-clot, removal of the neural arches, to relieve the pressure, may be advisable. Such surgical treatment could be adopted with least risk of ill effects in cases in which the hæmorrhage is extradural; but, unfortunately, these are the very cases in which the operation is least likely to be required, for it is rare to meet with compression symptoms from hæmorrhage in this situation. Yet even where there is reason to suppose that the hæmorrhage is intra-meningeal, surgical intervention is undoubtedly justified when life appears to be threatened by the effects of the compression; and even when this is not the case, but there is reason to suppose that irreparable damage is being done to the nerve-elements, the operation deserves our careful consideration.

For the treatment of meningitis, bed-sores, and cystitis, the reader is referred to other portions of this work.

Any residual paralysis and sensory disturbances must be treated on the recognised lines by massage, electricity, baths, gymnastics, and so forth. Of drugs, the iodides are most serviceable in the earlier stages, iron and strychnine later.

**II. INFLAMMATIONS.—1. External Spinal Pachymeningitis.**—This condition is also designated “peri-pachymeningitis,” or simply “peri-meningitis,” either name agreeing well with the state of things present in these cases; for the inflammatory process takes place in the loose cellular tissue which surrounds the dura, and occupies the space between this membrane and the bony wall of the neural canal. As in the cervical region the cellular tissue is more scanty and closer, this form of peri-meningitis rarely gives rise to any symptoms in connexion with the meninges of this part of the cord; moreover, there is no tendency for the process to spread to the intracranial cavity. The process may be diffuse, affecting a considerable extent of the long axis of the canal; or it may be more circumscribed, and limited to a small part of it. The process goes on to suppuration, and occasionally is found associated with a purulent leptomeningitis.

*Causation.*—In the vast majority of instances the process is secondary; indeed, it is very doubtful if it ever is primary.

(a) Spinal caries is responsible for no mean proportion of the cases;



abscesses originating in the bodies of the vertebrae make their way into the neural canal, or secondary inflammatory processes without pus occurring in the peridural cellular tissue find their way into this space directly from the bone. As a rule, this form of peri-meningitis is tuberculous; and a caseous condition may be met with, a thick layer of this material occupying the space between the bone and the dura, to the outer surface of which membrane it is intimately adherent. Sometimes fibrous-tissue proliferation is well marked, originating in granulation-tissue, and leading to the formation of thick masses. The leptomeninges may become affected secondarily.

(b) Inflammatory processes in the neighbourhood of the spinal canal, such as psoas abscesses and angina Ludovici. Pus may make its way into the neural canal by way of the intervertebral spaces, and thus set up a meningitis.

(c) Bed-sore.—Closely allied to the last mode of causation is the way in which this external meningitis may arise as a consequence of deep bed-sores which, extending down to the sacrum, may perforate into the lower part of the neural canal; and, in rarer circumstances, may even lead to a necrosis sufficiently extensive to lay bare the spinal cord.

(d) Trauma.—Contusion of the muscles of the lumbar region or loins, haematoma of the muscles of the back, and the like have all been known to lead to purulent peri-meningitis.

(e) Metastatic.—I once examined a case in which peri-meningitis, with pus formation and haemorrhagic extravasation, existed in the lower cervical and upper thoracic regions of the neural canal; it was associated with other evidences of septic conditions in other parts of the body: there was no disease of bone, or other local process, to account for the occurrence of the meningeal disease.

*Symptoms.*—As in all meningeal affections, pain in the back is a prominent symptom; but it varies a good deal in degree. It may be referred to the greater part of the length of the spine, or it may be felt chiefly in the loins, or between the shoulders. Lancinating pains may occur, and may be referred to the trunk or limbs, commonly giving rise to the girdle sensation. Stiffness of the back is also common; but it may not be so obvious as in many other affections of the meninges, as the part in which it can be most readily recognised, namely, the cervical region, is the very part of the neural canal which, as we have seen, is least commonly affected. It is not common to meet with spasms in the muscles of the limbs; they do occur, however, in some cases; yet usually even then they are only brought out, in any notable degree, on movement.

Motor paralysis may, of course, result from pressure on the spinal cord, and, as it is so rare for the cervical region to be affected, paraplegia of the legs is the most common form of paralysis. We are, of course, speaking of pressure on the spinal cord as a result of the peri-meningitis, not resulting directly from a common cause of the peri-meningitis, namely, spinal caries, which not infrequently affects the

cervical region, and may give rise to paralysis of all four limbs. It is worthy of note that the paralytic phenomena dependent on a perimeningitis may precede the symptoms already described as so characteristic of meningeal affections.

In association with the other phenomena of irritation, hyperaesthesia of the skin may be present, especially in the legs; but there may be anaesthesia, corresponding in distribution with the paraplegia.

The sphincters may be affected; the usual sequence of events being that retention of urine occurs first, and is followed by incontinence.

*Diagnosis.*—From what has been said with regard to the symptoms to which this condition gives rise, we can see how impossible it may be to distinguish this from any other form of meningitis; even if we bear in mind that paralysis is common, and occurs early in this variety, and that spasm of the neck is usually absent. There are certain signs, however, which may lead to a correct diagnosis in such cases; notably the discovery of any collection of pus in the neighbourhood of the spinal column, and again of any condition to which the affection is known to be secondary, such as spinal caries, angina Ludovici, a deep bed-sore with, perhaps, necrosis of the sacrum.

*Prognosis.*—As in many cases the diagnosis must of necessity be doubtful, it is difficult to estimate the proportion of cases which terminate favourably; for where recoveries occur there is no means of ascertaining whether the diagnosis had been correct or not; and, even of cases ending fatally, the number of necropsies published are not sufficient to support any very definite conclusions. In cases associated with spinal caries, the whole process may certainly become arrested, and even cured.

**2. Internal Haemorrhagic Pachymeningitis.**—This condition, also known as haematoma of the spinal dura mater, is rare; it is of the same nature as the haematoma which occurs in connexion with the cranial dura mater, with which condition, indeed, it is commonly associated.

*Causation.*—If we except trauma, all the conditions which give rise to this form of pachymeningitis do so in conjunction with a similar affection of the cranial dura. This is the case in general paralysis of the insane, and chronic alcoholism. A third condition with which internal haemorrhagic pachymeningitis may be associated is tuberculous meningitis, which, as we shall see, rarely exists apart from the same affection of the cerebral meninges.

*Morbid Anatomy.*—The inner surface of the spinal dura is covered by a fibrinous-looking membrane, which is comparatively easily separated from it, and in which haemorrhages of various sizes are seen. Parts of this membrane may be quite free from any extravasated blood, especially if the condition happen to be seen in its earliest stages. The extravasations are usually small, though large haematomas may occur. The blood may be encysted or undergoing transformation, when the false membrane with the contained blood presents various shades of brown, from

red to yellow. In some cases the whole length of the spinal dura is affected in this way ; in others, the process is partial, and may be limited to even a small part of the caudal end of the cord. This form of pachymeningitis may be associated with the external variety.

Occasionally adhesions form between the dura and pia-arachnoid ; but, on the other hand, the pia may be haemorrhagic in appearance only, from absorbed blood, or it may even be perfectly natural. The cerebrospinal fluid is blood-stained to a variable extent.

*Pathology.*—For the different views that have been advanced concerning the primary nature of the morbid process, the particular membrane in which it originates, and the source from which the haemorrhage is derived, the reader is referred to the article on cerebral haemorrhage in Vol. VIII. I will only say that Virchow's view—that the process is primarily inflammatory with secondary haemorrhages into the newly formed membrane—accords best with my experience. My observations also lead me to conclude that the primary seat of the affection is the dura mater, not the pia-arachnoid, as contended by Bondurant ; and, moreover, that the source of the haemorrhage, in the earlier stages at any rate, is the vessels of the dura mater.

*Symptoms.*—The symptoms are those of a subacute cerebrospinal meningitis, as there is concomitant affection of the cerebral meninges ; or the spinal symptoms may be quite overshadowed by the cerebral. When spinal symptoms can be detected they consist in pain in the back, pain radiating along the course of the nerve-roots, stiffness of the vertebral column, spasms of the muscles of the trunk and limbs, and perhaps hyperaesthesia and other signs of irritation.

*Diagnosis.*—Where symptoms, such as those that have just been narrated, come on in the course of general paralysis of the insane, or of chronic alcoholism, especially if accompanied by others referable to a similar condition of the cerebral membrane, the diagnosis may be made with comparative confidence.

*Treatment.*—The measures recommended in the treatment of haemorrhage into the spinal meninges are of service in these cases also (p. 593).

3. *Hypertrophic Cervical Meningitis.*—It is very doubtful whether this affection deserves to be described separately, or whether it would not be more correct to regard the clinical picture as the result of a more or less accidental limitation of a morbid process to the meninges of the cervical region of the spinal cord, which process, if affecting any other region, would of course give rise to a different picture. Further, it becomes a question whether any morbid condition of the meninges of the cervical region of the cord, resulting in its compression and in interference with the nerve-roots at this level, is not capable of producing a clinical picture indistinguishable from that which we have hitherto regarded as distinctive of hypertrophic cervical pachymeningitis, as represented to us chiefly by Charcot and by Joffroy. Nevertheless, as it has been customary to describe this condition separately, I propose thus to



deal with it; clearly recognising, however, that other morbid processes of the spinal meninges, similarly limited, are likewise capable of reproducing the clinical phenomena which are supposed to be characteristic of hypertrophic cervical pachymeningitis.

*Causation.*—There is considerable uncertainty as to the causes of this form of pachymeningitis, though it has usually been attributed to exposure to cold, to injury, or to over-exertion. There can be little question, however, that some of the cases owe their origin to syphilis; and to my mind this is one of the most potent arguments for regarding the condition as but a sub-group, for that syphilis may and does give rise to pachymeningitis of other regions of the spinal cord cannot be gainsaid.

*Morbid Anatomy.*—The hypertrophic thickening of the dura mater, which may be as much as 0·5 cm., is consequent on the deposition of concentric layers of fibrous tissue, the result of inflammatory proliferation of the membrane. The greatest thickening usually occurs on the posterior aspect; and here the dura becomes adherent to the periosteum of the neural arches, and to the posterior vertebral ligament. The dura is also intimately united with the pia-arachnoid; so that it is quite impossible to separate the different membranes from each other. The thickened dura is sometimes very tough; and the appearance may suggest the formation of an outer and an inner layer. The walls of the vessels are thickened.

By the pressure the spinal cord is flattened dorso-ventrally; moreover, inflammatory and other changes are met with in its substance, especially at the periphery. Here there is a marginal sclerosis in which several factors are probably operative; foremost among them may be the spread of inflammation from the meninges to the cord along the septa of the pia mater, and along the vessels; but direct pressure on the periphery of the cord—with consequent destruction of the marginal nerve-elements, interference with the vascular supply by compression of the pial vessels, and hindrance to lymph flow by similar compression of the lymph channels—must be a concomitant factor. A diffuse myelitis, thus initiated, extends for a varying distance into the substance of the cord, especially affecting the posterior and lateral columns, and leading to secondary ascending and descending degenerations. The process may, however, become more extensive, affecting the cord throughout its whole thickness, and giving rise to considerable sclerosis with consecutive atrophy. There is much to be said for Köppen's view that only the marginal changes in the spinal cord are to be attributed to the thickened membranes; and that the inflammatory changes in the cord may owe their origin to the action on the interstitial tissue of the same cause which induced the meningeal affection. This view appears to me to be specially applicable to those cases in which syphilis seems surely responsible for the vascular and sclerotic changes in the meninges and in the cord itself. Other changes in the cord substance, met with in some instances, consist in softening, even to excavation. The nerve-roots are compressed and



show degeneration of the nerve-fibres, with proliferation of the interstitial tissue.

*Symptoms.*—The clinical course of the affection, in conformity with the teaching of Charcot, may be described in three stages.

Pain is the leading feature of the first period; it is exceedingly severe and is referred to the neck, spreading up even over the occipital region to the vertex, and also radiating downwards into the arms, in the larger joints of which it is often seated. Though present, as a rule, in some degree, it is prone to paroxysmal exacerbations, when the suffering may be intense. There may be a feeling of constriction in the upper part of the thorax, and various paraesthesias are common in the arms. Moreover, herpes may appear in the distribution of some of the irritated nerve-roots. Movements of the head and upper limbs increase the pain, and tenderness is provoked by any pressure or percussion on the cervical spines. There is rigidity of the cervical muscles, with stiffness of the neck, as in cervical caries, this condition being reflex in part, and in part the result of voluntary effort to prevent the increase of pain on movement. This period of the affection is thus marked by the phenomena of nerve-root irritation; it usually lasts for two to three months. Apart from the rigidity of the muscles of the neck, and more or less perhaps of the arms, the motor functions are little interfered with during this stage; though a slight degree of weakness and some twitching of the muscles of the upper extremities may be noted.

The second stage is characterised by paralysis and atrophy of certain muscles of the upper limbs consequent on extension of the morbid process to the anterior nerve-roots. The muscles supplied by the median and ulnar nerves are thus affected; those supplied by the posterior interosseous escape altogether, or are affected in slight degree only, or not until late in the affection. The atrophy of the muscles becomes pronounced, and on electrical examination they shew the reaction of degeneration. As the flexors are considerably affected whilst the extensors escape, unopposed action of the latter results in hyper-extension of the hand at the wrist, with extension of the first phalanges, and flexion of the second and third; this gives rise to a peculiar position of the hand called the "preacher's hand": this position of the hand, however, is neither constant in cases of hypertrophic cervical pachymeningitis, nor peculiar to it, as Charcot was aware. In addition to the loss of certain movements consequent on the affection of the groups of muscles already referred to, there is a varying degree of general enfeeblement of the arms from the shoulders downwards; sometimes it is no more than a general stiffness and clumsiness of execution, but at other times it amounts to complete paralysis of one or both limbs.

The severe pain of the first stage of the affection is much mitigated during the second period, though the paracesthesias usually persist and even increase. Anaesthesia, consequent on destruction of the sensory nerve-roots, now appears, in a manner comparable to the muscular atrophy which results from destruction of the motor roots; and, as in the latter

case, this does not pervade the skin of the whole arm, but only that corresponding to the distribution of certain roots. This sensory defect is a further factor which interferes with movement, more especially with the finer movements of the fingers; so that the picking up of small objects, for instance, is clumsy.

The third stage is characterised by phenomena consequent on compression of the spinal cord; by spastic paraplegia without muscular atrophy, but later by contracture; anaesthesia may become manifest in the legs and trunk, the functions of the bladder and rectum may be interfered with, and bed-sore, if not prevented, may soon follow.

Pain, such a prominent feature of the first stage, usually disappears before the third stage is reached, when paralytic phenomena, as a rule, completely replace those due to irritation of the sensory nerve-roots.

It remains to be said that whilst the above description forms the type of the affection, many variations in its course are met with. I have said that the characteristic position of the hand may not be present; the patient may be spared the intense suffering caused by pain in the earlier stages; and affection of the lower limbs, bladder, and rectum may be met with quite early in the course of the malady.

The disease always extends over several years, death usually resulting from the consequences of cystitis, or from bed-sore.

*Diagnosis.*—As the same symptom-group may be anticipated in any chronic meningo-myelitic process of this part of the cervical cord, however induced, it follows that considerable difficulty may attend the diagnosis. The several affections with which the condition may be confounded depend on the stage at which the case is seen.

However much we may suspect that the pain of the earliest stage is consequent on irritation of the posterior roots by some organic process in the meninges, it may be impossible to exclude with certainty its dependence on an idiopathic neuralgia; or, again, where girdle sensation is well marked, it may be difficult to exclude tabes, and even more so to decide that, of all organic processes of the meninges possible in this region, that which we are now considering is the one present. It is the appearance of loss of motor power with muscular atrophy of root distribution which serves satisfactorily to answer the first of these questions; yet even then the second, concerning the nature of the morbid process, may be no nearer a satisfactory solution. Syphilitic meningo-myelitis, cervical caries, and tumours in the cervical region of the cord may all result in paralysis with muscular atrophy, which has been preceded by pain and other phenomena indicative of irritation of sensory roots. Of these it may be possible to distinguish cervical caries by means of an *x*-ray examination of the spine, angular curvature which never occurs in the meningeal affection, tenderness greater in degree than is usual in pachymeningitis, evoked by pressure over a single vertebra, early in the course of the affection; and by the detection of tuberculous mischief in other organs. Yet all these signs may be absent, and the case may turn out to be one of caries after all.

As the symptoms produced by a pachymeningitis really depend on the meningo-myelitis, and as syphilis plays an important part in many cases of hypertrophic cervical pachymeningitis, it is obvious that even a syphilitic history does not help us to discriminate between this condition and syphilitic meningo-myelitis. If Wassermann's serum test proves positive and an examination of the cerebrospinal fluid reveals an excess of lymphocytes, it would be idle to deny the syphilitic origin of the process. A further point in diagnosis is that a syphilitic affection of the meninges and cord is not wont to remain limited to any one region; so that, while commonly affecting the cervical part of the cord, it may shew evidences nevertheless of invasion of other levels, a state of things less likely to be met with in the pachymeningitis of Charcot.

Where, as I have seen, new growth infiltrates the dura so as to produce a condition in all respects comparable with a hypertrophic pachymeningitis, symptoms of symmetrical implications of the nerve-roots and spinal cord make it quite impossible, in the absence of evidence of new growth elsewhere in the body, to arrive at a correct diagnosis. Though far from an infallible indication, symptoms of unilateral disease of nerve-roots and pressure on the spinal cord lend weight to the probability of tumour, as opposed to pachymeningitis. The rate of progress may aid us, for the course of a pachymeningitis is slower, as a rule, than that of a tumour; but here, again, there are notable exceptions which rob this indication of much of the value it would otherwise have. The problem may, however, remain unsolved unless lumbar puncture reveals meningitis as evidenced by turbidity and lymphocytosis of the cerebrospinal fluid.

Syringomyelia begins, as a rule, in the cervical region, and as it produces muscular atrophy and weakness of the upper limbs, with, it may be, spastic phenomena in the lower, and as, moreover, pain may be a prominent feature in this disease, its exclusion in a differential diagnosis may be attended with very great difficulty. In syringomyelia, while tactile impressions are normally perceived, painful and thermic impressions are unfelt; this sign may, however, be absent in syringomyelia, and it has been present in some cases of pachymeningitis. The presence of painless whitlows and other trophic disturbances of the skin, and the existence of lateral curvature, are points in favour of syringomyelia. The course of the latter disease, again, is much more protracted, extending, as a rule, over a period of a great many years. As further aids to the diagnosis of syringomyelia, careful inquiry should be made, in the past history of the patient, for indifference to taking hold of hot things; for burns that were not painful, for operations painless without an anaesthetic. Careful search should also be made for scars suggestive of former burns or operations.

Although the distribution of the muscular atrophy and weakness in the arms could be explained equally well by a progressive muscular atrophy, and while the added spastic phenomena in the lower limbs suggest an amyotrophic lateral sclerosis, the complete absence of sensory



disturbances in these conditions, whether irritative or paralytic, serves to exclude them. In any case the subsequent course of the case will settle the question; for, whereas in progressive muscular atrophy and amyotrophic lateral sclerosis there may be a spread of the disease to the medulla, giving rise to bulbar symptoms, this never occurs in hypertrophic cervical pachymeningitis.

In local neuritis the muscular and sensory defects correspond to nerve and not to root distribution; moreover, there is tenderness, and, it may be, thickening of the nerve-trunks, and an absence of pain and stiffness in the neck. It may be difficult, however, in the absence of any phenomena indicating pressure on the spinal cord, to exclude a neuritis of the cervical roots. In multiple neuritis a cause can usually be found in the shape of some toxic agent, notably alcohol, lead, or arsenic. Tenderness in the course of the nerves, and flaccid paralysis, in which the extensors suffer more than the flexors (the reverse of what obtains in hypertrophic pachymeningitis), with abolition of the tendon-jerks both in the superior and inferior extremities, serve to distinguish these conditions; excepting in cases of lead neuritis, in which a certain degree of spasticity with exaltation of the tendon-jerks may be present in the lower extremities. Concomitant evidence, in the shape of a history of lead intoxication, colic, the presence of the blue line along the gums, and the absence of any anaesthesia, serves to distinguish these cases.

*Treatment.*—Various measures may be tried for the relief of this disease; but, as a rule, some palliation is all we can expect. Counter-irritation to the spine is indicated; the milder forms of this, such as painting with iodine liniment, are of little use; the more energetic forms of counter-irritation are called for, such as repeated blisters, or Paquelin's or the actual cautery, which latter means is especially recommended by Joffroy. In any case iodide of potassium should be given, and if there is any suspicion of syphilis, it may be advantageously combined with mercurial treatment. Where the evidence is in favour of syphilis a course of treatment by inunction, as in syphilitic meningo-myelitis, should be carried out.

Warm baths and diaphoretic measures are of service; and for the wasting muscles massage and electrical treatment should be employed.

4. Syphilitic Meningo-myelitis (see Article "Syphilis of the Spinal Cord and Membranes," p. 726).

5. **Leptomeningitis.**—A. **Acute Leptomeningitis.**—*SYN.*: *Acute internal meningitis, Simple meningitis, Purulent meningitis.*—In this condition the inflammatory process involves the arachnoid and pia as a rule; and in many cases the inner surface of the dura mater is affected also. According to some observers the process may, in rare instances, be limited to the arachnoid, without involving the pia.

The following account of the affection will not include epidemic cerebrospinal meningitis, which has already been dealt with (see Vol. I.



p. 923); acute tuberculous spinal meningitis will be reserved for subsequent brief consideration (p. 613).

*Causation.*—Having excluded the epidemic cerebrospinal and tuberculous forms of acute meningitis, we are left with the following etiological factors, each of which appears capable of inducing a meningitis :—

(i.) Purulent cerebral meningitis, especially when affecting the base of the brain, is prone to extend to the spinal meninges.

A purulent process in connexion with the spinal column, as in spinal caries, or an abscess of the soft parts in the neighbourhood of the spine may cause it; as may a deep bed-sore over the sacrum perforating into the neural canal. Suppurations in the pleura and mediastinum are said to have extended in like manner to the spinal meninges. On the other hand, the infective agent may be derived from some distant collection of pus or septic inflammation, as in pelvic suppuration (whether the result of puerperal infection or not); from cystitis, however induced, but especially when gonorrhoeal; from a gonorrhoea without cystitis; or from a pyelitis. Similarly empyema, abscess of the lungs, and bronchiectasis may supply the infective agent, as may suppuration in any other organ. Carbuncle of the neck or back not uncommonly leads to a meningitis.

(ii.) A spinal meningitis may arise in the course of an infective disease, such as infective endocarditis, septicaemia, and erysipelas; in connexion with the acute exanthems, pneumonia, rheumatic or enteric fever.

(iii.) In sporadic cases of epidemic cerebrospinal meningitis the mischief is sometimes restricted to the spinal cord. Such cases are of more moderate intensity than in the epidemic form. Although isolated instances occur, sometimes the number of such cases increases to such an extent as almost to constitute an epidemic.

(iv.) Injury, whether it be an injury to the spinal column or not, may lead to a meningitis. Without any fracture of the spine there may be tearing or contusion of the meninges; or injury to the spinal cord itself may form a suitable nidus for the multiplication of micro-organisms, which in their turn may give rise to meningitis, in association, it may be, with myelitis. The microbes may gain an entrance, in such circumstances, by way of an external wound; or, without any such, they may be derived from the intestinal or pulmonary tracts. In this category must be mentioned operative procedures on the spine, and notably that for spina bifida, which formerly was often attended with this result; or a spina bifida may be responsible for a meningitis by rupture of the sac.

(v.) Cold is said to cause meningitis; and instances have been recorded in which this result has come about as an immediate consequence of great lowering of the surface temperature of the body, as from falling into water or sleeping in the open air. It is probable that the cold only acts as a general depressing influence, creating a place of less resistance of which micro-organisms take advantage.

*Morbid Anatomy.*—There is a good deal of variation in the extent of

the spinal meninges affected in the long axis of the cord. In cases in which the inflammation has extended from the cranial cavity, only the upper few inches of the spinal meninges may shew any change; or evidences of meningitis may be found as low down as some point corresponding to a change of direction in the spinal column, from a position more or less vertical above to one horizontal below, as the patient lay in bed. Herein we see how important is the part which gravity plays in the extension of the morbid process. If seen early in traumatic cases in which there has been injury to the bones, or in cases of caries, or in abscess of the spinal cord, the meningitis may be limited in extent; but in all these cases the tendency is for rapid spread to occur from the seat of origin. In sporadic inflammation of an infective character the whole longitudinal extent of the meninges is usually affected, the morbid influence making itself felt simultaneously in all parts of the meninges; but even in these cases, as in all others in which the membranes are involved in their whole extent, the evidences of inflammation are, as a rule, most marked on the dorsal aspect of the cord. No doubt gravity has much to do with this result, the recumbent posture facilitating the backward flow of the exudation whose ingredients are capable of inducing or increasing the inflammatory irritation.

As stated, the inner surface of the dura mater may be concomitantly affected; and, strange as it may seem, the pia, though usually affected in conjunction with the arachnoid, sometimes escapes; in these circumstances the spinal cord is also unaffected, but otherwise a varying degree of secondary affection of the spinal cord results. The nerve-roots are, of course, liable also to secondary implication; but so great is their power of resistance that it is surprising how little change they may shew even when bathed in pus; indeed, in these circumstances they sometimes appear quite intact.

The morbid appearances depend a good deal on the length of time between the onset of symptoms and the death of the patient. In its earliest stages the membranes may only shew pronounced hyperaemia, accompanied perhaps by punctate extravasations of blood. Similar appearances may be met with on the inner surface of the dura mater and in the spinal cord. Even at this stage the cerebrospinal fluid is cloudy. It is rare to meet on necropsy with these early indications of meningitis alone; far more commonly the disease has passed beyond this stage, so that there are added evidences of a more advanced inflammation. Now the leptomeninges are of a milky appearance, or more opaque, and distinctly thickened; and there is distinct exudation bathing the outer surface of the arachnoid, lying in the meshes of this membrane, and occupying the space between it and the pia. All degrees of turbidity of this exudate are seen, up to the most definite formation of pus, greenish-yellow in colour and creamy in consistence. Even before such visible evidence of pus, microscopical examination of the turbid exudate, or of the meninges, reveals pus-cells in abundance; a state of things that may be found also in the pia and the inner layers of the dura. Moreover, the

sheaths of the engorged vessels are infiltrated with similar cells. Although the nerve-roots frequently escape damage, even in purulent meningitis, they may, when affected, shew naked-eye evidences of this, in the shape of swelling and redness; and on microscopical examination round-celled infiltration is seen in conjunction with destruction of the nerve-elements. Spread of the inflammatory mischief to the spinal cord always takes place where the pia mater is affected; and the changes then met with are those of a myelitis chiefly affecting the periphery of the cord, and extending more deeply into its substance, in wedge-shaped patches with their apices directed inwards and their bases fusing at the periphery. Such extension into the deeper parts of the cord results from spread of the inflammatory products along the perivascular spaces of the pial vessels which dip into and supply the substance of the cord for a considerable depth. In some cases, however, instead of finding a myelitis having so distinctly a marginal distribution, we may meet with irregularly scattered minute foci of inflammation, as in the case recorded by Dr. T. Buzzard and myself. In such cases it is probable that the myelitis and the meningitis are produced independently by the same causative agent; or it may even be that in some of these cases the myelitis may be primary in point of time, and the meningitis induced secondarily by extension of the inflammatory process to the surface of the cord at various parts. When the cord is involved, softening and other macroscopic and microscopic changes common to myelitis are met with, and need not be described here. On the other hand, the spinal cord may be intact, even in the presence of a purulent meningitis, provided the pia be not involved. The cerebrospinal fluid is increased in amount, is turbid, and contains flocculi of pus.

Bacteriological examinations in these cases yield results, as regards particular micro-organisms, which vary with the cause of the meningitis. The ordinary pus cocci are commonly met with; but other organisms have also been found, notably the diplococcus of pneumonia; and in the case to which I have already referred, we found a diplococcus, pathogenetic to animals and having certain resemblances to the *Diplococcus intracellularis* of Weichselbaum, and to that of simple "posterior-basis" meningitis described by Prof. Still, though in certain particulars differing from both of these organisms. The micro-organisms are found in the exudation, in the meninges, in the cord itself, and in the cerebrospinal fluid; from all of which sources they may be cultivated on artificial media: or on microscopical examination they may be detected after suitable staining agents have brought them into view. In the case of the *D. intracellularis* the micro-organisms may be met with in the cells of the exudate; but otherwise the organisms lie free outside the cells, and in the tissues: they are especially plentiful in the immediate neighbourhood of the vessels, the perivascular spaces sometimes containing large numbers of them; or they may even be met with in the interior of the vessels themselves, in the smaller branches of which they may produce embolic obstruction.



If, instead of death during the acute stage of the inflammatory disturbance, the patient survive, absorption of the inflammatory products takes place; but permanent changes remain by which the disease may be recognised on a subsequent necropsy. The meninges are cloudy and thickened, usually in an irregular manner; and a varying degree of matting together and adhesion is met with, not only of the arachnoid to the pia, but also of the former to the inner surface of the dura, and of the latter to the spinal cord. There is permanent excess of cerebrospinal fluid in the arachnoid space; and a collection of this, shut in by adhesions, may give rise to the appearance known as hydrocephalus.

When the spinal cord has been invaded, there will be a varying degree of sclerosis, diffuse or circumscribed, corresponding to the parts previously damaged by the myelitic process; and, extending from these areas, ascending and descending secondary degenerations, the precise amount of which will depend on the degree to which the afferent and efferent tracts have been involved in the primary process.

Apart from epidemic cerebrospinal meningitis, evidences of inflammation of the cerebral meninges are commonly associated with the spinal affection. Sometimes this is due, of course, to spread of the inflammatory process from the cerebral to the spinal meninges; but in others the reverse obtains, the spinal meninges being the primary seat of mischief. In some such cases there is no difficulty in tracing the continuity between the process in the neural canal and that in the intracranial cavity; in others the evidences of mischief in the membranes of the upper part of the cord are very indistinct, while the degree of meningitis, both below this and at the base of the brain, is much greater. The explanation of this probably is that the cerebrospinal fluid is the means of conveying the infection to the cerebral meninges. Where the cerebral meninges are invaded secondarily to those of the spinal cord, the mischief is always most marked at the base of the brain, and especially at its posterior part. Some slight extension along the lower part of the convexity of the hemispheres may be met with; but well-marked meningitis at the upper part of the convexity is very rare in such circumstances.

*Symptoms.*—It will now be readily understood that, apart from the concomitant occurrence of symptoms due to invasion of structures within the cranial cavity, the clinical manifestations of the spinal condition may vary considerably, according as those which indicate affection of the meninges, irritation or destruction of the nerve-roots, or invasion of the spinal cord predominate. As the manifestations of the last group are those of a myelitis to which meningitic symptoms are added, it would be superfluous to give a separate description of them here (*vide* p. 652); I propose therefore to confine my attention to the phenomena which indicate affection of the meninges, inseparable from which are those due to irritation and, it may be, subsequent destruction of the nerve-roots.

Premonitory symptoms, such as malaise and slight pain in the back, may precede the more characteristic symptoms of the condition, which consist in the acute and severe pain in the back in association with a



rigor and elevation of temperature. The seat of the pain varies with the seat of the morbid process, but is frequently referred to the whole length of the spine; even then, however, it may be more intense at certain points than at others. This pain is often of the most violent character, and makes even the slightest movement of the patient quite unbearable; although constant it is prone to acute exacerbation. It is due, no doubt, to irritation of the nerves of the inflamed meninges. Pressure on the spinous processes of the vertebrae elicits tenderness over the seat of the inflammation, and a hot sponge applied to the skin of the back increases the pain.

Pain of a different character is also present, which is distinctly referable to irritation of the sensory spinal nerve-roots. The pain is sharp, lancinating, or tearing in character; or again burning or constricting; this on the trunk gives rise to the well-known girdle-sensation. It is paroxysmal, and radiates in the areas of distribution of the sensory roots of the trunk, or limbs, or both; according as the seat of the mischief in the meninges allows of irritation of one or both sets of nerve-roots. The skin areas, corresponding to the distribution of these irritated sensory roots, may become markedly hyperaesthetic; and herpetic eruptions may appear in such areas. There is also tenderness of the muscles on pressure; this is especially marked in the legs, where it may be present when no discomfort results from similar pressure of the muscles of the arms. Interference with the vasomotor nerves causes the hyperaemia, which appears on stroking the skin with the finger-nail or a pin, to be excessive in degree and to persist for an undue length of time, the phenomenon being known as the *tache spinale* or meningeal streak.

Equally characteristic of meningitis is the muscular spasm which usually accompanies the pain, and gives rise to varying degrees of rigidity, more especially of the neck and back, but it may be of the limbs also. The rigidity may be restricted to a small part of the back corresponding to the seat of inflammation, or the whole of the back muscles may be affected in a meningitis of more extensive distribution, giving rise to the most pronounced opisthotonos. Even if the whole back be not thus attacked, there may be notable arching back of the neck, so that the occiput comes into close contact with the nape of the neck; and even when the rigidity afterwards becomes more general, it is often noticed first in the neck. The other trunk muscles commonly become involved, including those of the abdomen, spasm of which results in a boat-shaped retraction of the abdominal walls. The muscles of the limbs also become rigid, and paroxysms of painful recurring spasms occur in them, either spontaneously or on any attempts at movement. A rapid rhythmical tremor of the limbs may also occur; both this and the previous symptom are more commonly observed in the arms, whilst the legs may be persistently flexed at the knee, the patient being unable to overcome this contraction of the hamstring muscles. Some of the rigidity of the back may be in part the result of voluntary efforts to keep the spinal column fixed, owing to the intense suffering caused by the slightest movement;

but a more important factor in this spasm, as well as in that of other parts of the trunk and the limbs, is irritation of the sensory nerve-roots and the nerves of the meninges bringing about the spasm reflexly, whilst irritation of the motor roots brings it about directly.

In the early stages of the disease the reflexes are increased. There is spasmodic retention of urine, with irritable attempts on the part of the detrusor to expel the contents of the bladder. Constipation is usually troublesome. There is always some pyrexia, though this may be insignificant. The pulse is either rapid or abnormally slow. Respiration may be interfered with by spasm of the thoracic muscles so far as to cause dyspnoea, which may even become urgent.

When the cerebral meninges are involved, there is headache, delirium, or somnolence passing on to coma; an event which may or may not be preceded by convulsions. Cheyne-Stokes breathing may occur in consequence of extension of the mischief to the medulla. The functions of some of the cerebral nerves may become disturbed, and notably squints, either irritative or paralytic, may appear.

The further progress of the case, in so far as the spinal symptoms are concerned, is marked by the subsidence of the signs of irritation, and their replacement by others indicative of destructive processes in the spinal cord and the nerve-roots; though, owing to the great power of resistance which the nerve-roots possess, evidences of the latter condition are rare. The anaesthesia and muscular atrophy of root distribution are therefore rare; and the anaesthesia with motor paralysis is to be attributed to extension of the mischief to the spinal cord; and the latter may become so great that scarcely any movement can be performed. As a rule the paralysis is at first of the spastic type, with exaggerated knee-jerks and ankle-clonus; but in severe cases, and especially where the grey matter of the cervical and lumbar enlargements is invaded, flaccidity follows, and the tendon-jerks are abolished. In such circumstances it becomes a matter of difficulty to decide how much is to be accounted for by affection of the spinal cord, and how much may be due to destruction of nerve-roots. Vasomotor disturbances may be intense, so that even a slight prick or scratch may cause a large wheal to rise at the seat of irritation. Large bullae may result from slight pressure on the skin, as by one leg lying for even a short time against its fellow; and bed-sores are apt to appear. There may be considerable pyrexia; the heart becomes feeble; and death may result from asthenia, or from paralysis of the muscles of respiration.

Instead of this rapidly fatal course there may be abatement in the severity of the symptoms; though the general tendency may still be that of slow progress in the wrong direction, suffering being thus prolonged, and death resulting after some weeks from bed-sore, or from renal disease secondary to cystitis. In less severe cases, however, the irritation may gradually subside, and recovery may come about; though evidence of permanent damage to the spinal cord remains in the shape of anaesthesia and muscular paralysis, it may be with contracture or with

muscular atrophy consequent on damage to the cord or nerve-roots. Unfortunately, in some cases in which the residual effects point to but slight permanent damage to the spinal cord, there may be subsequent increase of symptoms due to a chronic myelitis following the acute mischief. Then the best that can usually be hoped for is recovery with some persistence of spastic paraplegia, with or without some disturbance of the function of the bladder; yet in rare cases, in which the disease has been slight, complete recovery may result.

The distribution of the symptoms which characterise an acute meningitis depends on the seat of the process and on its extent. In the majority of instances the affection of the meninges is widespread, and the symptoms are correspondingly wide in range; but in other cases the inflammatory mischief is circumscribed, and the symptoms are likewise limited, though not necessarily to the same extent as the morbid process on which they depend. When such circumscribed meningitis exists in the cervical region, prominent among the manifestations are those in connexion with the upper limbs; respiration may be seriously interfered with, even to the degree of urgent dyspnoea. Dilatation or contraction of one or both pupils, with narrowing of the palpebral fissures, may be the result of interference with the pupillary fibres of the sympathetic. Deglutition often becomes very difficult, and the heart's action may be disturbed. When the thoracic region is chiefly affected, the pain and spasm are usually most marked in the trunk; though similar phenomena may also be met with in the lower limbs. And when the chief seat of the mischief is in the lumbar region, the symptoms are confined to the loins and lower extremities. Spread of the inflammation to the cerebral meninges is signalled by headache, vomiting, delirium, and even convulsions. Interference with the functions of various of the cranial nerves may result, notably those supplying the ocular muscles; but the earliest to suffer are, as might be expected, the spinal accessory and hypoglossal.

The *course* of the disease varies; but, as a rule, it is rapid, all the symptoms reaching a high degree of intensity, in severe cases, within twenty-four to forty-eight hours, and ending in death in a few days. Such a result is usually due to implication of the cerebral meninges leading to paralysis of the heart or asphyxia. In less severe cases the acute symptoms persist for a few weeks, and then end either in death or recovery; in others months elapse during which evidences of slow destructive processes going on in the spinal cord appear.

*Diagnosis.*—In lumbar puncture we have a ready and certain means of diagnosing spinal meningitis. Even without this, little difficulty is likely to be found in the diagnosis of a typical case of acute meningitis; pain in the back, rigidity of the neck and back, retraction of the head and opisthotonos, hyperaesthesia of the skin, and spasm of the muscles of the limbs coming on acutely and in association with pyrexia, leave no room for doubt as to the nature of the case. Evidence of irritation preceding paralytic symptoms is all-important in the diagnosis; and it is graver, of course, when symptoms indicative of cerebral meningitis



coexist with those attributable to the spinal meninges. Further support is given to the diagnosis when a recognised cause for the meningitis can be established ; when, for example, symptoms such as those detailed above come on in the course of one of the acute infective fevers, or when some purulent affection exists in some other organ, and is thus a possible source of infection, or where an injury preceded the onset of symptoms. The chief difficulty is when symptoms of irritation are absent, as is so often the case in the secondary purulent variety, in which, as we have seen, the nerve-elements are usually but little disturbed.

As trauma may occasion either a haemorrhage into the spinal meninges or an inflammation of these structures, and as the former of these conditions may be followed by the latter in the same case, whilst, moreover, the manifestations of a haemorrhachis of necessity resemble those of a meningitis, the diagnosis may present some difficulties. Reliance must be placed on the sudden occurrence of the symptoms, which, in the case of haemorrhachis, rapidly reach their height without the occurrence of pyrexia ; whilst when due to meningitis, whether alone or following a haemorrhage, such symptoms do not make their appearance until two or three days after the accident, and they are attended with pyrexia.

It is unlikely that a haemorrhage into the spinal cord itself can be mistaken for a meningitis ; for the two conditions have nothing in common, except pain in the back, which, in the case of haematomyelia, is limited to one spot. The sudden onset with pronounced paralytic phenomena should prevent any possibility of error.

Similarly, there is comparatively little difficulty in distinguishing a myelitis uncomplicated with meningitis from a meningitis uncomplicated with myelitis. In the former case pain in the back is either absent or but slight ; there is an absence of spasm in the muscles of the limbs in the earliest stage ; and paralysis of motion, and it may be of sensation also, is the prominent feature of the case from the outset. But, as meningitis and myelitis commonly occur together, sometimes one and sometimes the other being the primary affection, it will readily be understood how difficult it may be to arrive at a differential diagnosis in such cases. Whenever severe pain in the back exists, especially if accompanied by rigidity, we may feel sure that we are dealing with a meningitis, whether we have evidence of the coexistence of a myelitis or not ; but where such symptoms precede those of a paralytic character the meningitis is the primary process.

The distinction of meningitis from tetanus must be based on the frequent absence of pyrexia in the latter condition, especially in its initial stage ; on the increase of reflex irritability to a much greater degree, so that lightly stroking the patient's skin or even walking towards his bed is sufficient to evoke severe spasms, whereas in meningitis the spasms usually come on when the patient tries to move ; and on the early occurrence of trismus. If the spinal meningitis be complicated by inflammation of the cerebral meninges trismus may occur, but in such circumstances it usually manifests itself much later than in tetanus ;



moreover, in tetanus this symptom is not accompanied by others of cerebral origin, such as delirium, convulsions, and coma. Any pain present in tetanus is due to the muscular spasm; there is an absence of radiating pains, of subjective sensations, and of hyperaesthesia of the skin.

Rheumatism of the muscles of the back may cause stiffness and pain on movement; and in children, if it is acute in onset and affects the cervical muscles, causing retraction of the head, the diagnosis may be difficult; but severe spontaneous and radiating pains are absent, and there is no spread of the spasm to the muscles of the limbs.

When hysteria simulates meningitis it is usually the cerebral rather than the spinal form which is manifested; in which case headache, vomiting, convulsions, and even what appears to be coma may be met with. Moreover, the pulse may become slow, and there may be spasm in the muscles of the back of the neck. Such cases may present a good deal of difficulty; but those experienced in the recognition of hysteria will, as a rule, be able to detect indications pointing to its existence, without the need for lumbar puncture; notably that sleep is natural, the coma is factitious, and the various manifestations may be influenced psychically.

Having decided that meningitis is present, much difficulty may still be experienced in deciding the form of the affection, unless lumbar puncture be employed. The recognition of the cause of the meningitis is all-important; thus when it occurs in the puerperal state, or in circumstances which favour the development of septicaemia, the purulent form is surely present. The onset is abrupt in these cases, and the manifestations, as a rule, stormy. In the tuberculous variety, on the other hand, there may be evidence of tuberculous disease in other organs, or a family history of such disease may be elicited; the onset is gradual, with indefinite symptoms at first, and, moreover, the coexistence of cerebral meningitis gives rise to symptoms which usually precede those of spinal origin.

*Prognosis.*—The prognosis is always grave, except in those cases which, though occurring sporadically, resemble the epidemic cerebrospinal form of the disease; in them recovery, either complete or partial, occurs in a large number of instances. The probable cause of the meningitis is a much better guide in prognosis than is the probable extent of the mischief; though, as far as the question of complete recovery is concerned, evidence of the degree to which the spinal cord is damaged secondarily is all-important. In the purulent form death is common, whether secondary to some suppurative process about the spinal column, or metastatic in origin, the source of infection being situated at a distance. The prognosis is very bad in those cases which follow the acute infective fevers, or tuberculosis; and it is also serious in cases resulting from severe lesions of the spinal column, though in cases which are consequent upon the slighter traumatic influences the prognosis is much better; as it is also in those cases in which cold appears to be the cause of the meningitis.

Although the causation is the most important factor in prognosis,

valuable aid is obtained from other considerations; thus, the higher the temperature, the more acutely the symptoms come on, and the more severe they become, the more serious the prognosis; and the early substitution of paralytic for irritative phenomena is of equally grave import. The prognosis further depends on the stage at which the case is seen; thus, it becomes better if some days have elapsed since the onset; especially if there be any signs of abatement of the disease, such as diminution of pain and pyrexia, without the appearance of paralysis. Prognosis has to be guarded, however, even at this stage, in view of the many complications that may arise, and owing to the frequency of relapses; moreover, if paralytic phenomena are present, though life may be spared, the patient may be crippled by the persistence of this in association with spasticity or muscular atrophy. The age of the patient influences prognosis, as does his former state of health also; the chances of recovery are less in children and in old people than in adults at and below middle life; and debilitated subjects run a poorer chance than persons previously robust.

*Treatment.*—It is of primary importance that the patient should be kept at rest on a smooth water-bed; and, although it is harmful to have the back the most dependent part, this cannot well be avoided in most cases, as both the lateral and prone positions require a certain degree of muscular effort, sufficient, as a rule, to evoke attacks of spasm, which do more harm than the results of gravitation. Moreover, the prone position may seriously impede respiration in cases in which the meninges of the upper parts of the cord are affected. Provided the spasms are not made worse to any extent, and that there is no reason to fear failure of respiration, the prone or lateral positions are to be preferred to the dorsal. Mental as well as physical rest should be secured; the room should be cool and airy, darkened, and kept as quiet as possible. The greatest possible care is necessary to prevent the formation of bed-sores, the most scrupulous cleanliness being called for in the nursing of such cases. The strength must be kept up by nourishing food, which, however, should not be stimulating; alcohol ought not to be given unless collapse threaten; and, though various mineral and other waters are allowed, where there is any weakness of the muscles of respiration the effervescing waters must be cautiously used, lest abdominal distension should seriously hamper the action of these muscles. When deglutition is difficult, especially in children, it may be necessary to administer nourishment by the nasal tube. The bowels should, of course, be kept freely open.

Hydrotherapeutic measures are of advantage in some cases, if employed early in the course of the disease; and are especially indicated where the attack seemed to be due to exposure to cold. In such cases free diaphoresis should be induced at the outset, by means of hot-air or vapour baths; or wet packing may follow an ordinary warm bath. Packing may be employed with advantage later in the course of the disease when the warm bath is contra-indicated on account of the pain and spasm induced by movement. After all acute manifestations have

subsided, and a more or less chronic stage of the affection is reached, bath treatment at Bath or Aix-les-Bains is of advantage.

Various local measures to the spine have been tried with a view to lessen the severity of the process within the neural canal. In the earliest stages dry and wet cupping are of advantage; the latter and leeching being, however, permissible in robust patients only. The practice of different physicians varies with regard to the use of heat or cold to the spine; but in cases of traumatic origin it will be found of most advantage on the whole to employ the latter in the shape of the ice-bag, especially when we suspect the existence of hæmorrhage; in other cases warmth is generally found to afford most comfort. Blistering and similar methods of counter-irritation should be avoided in the earlier stages of the disease; they may, however, prove useful later.

The only drug that appears to have any influence on the acute process is mercury, which may be given by inunction, or by the mouth; but the former method is far superior to the latter. Half a dram to a dram of blue ointment should be rubbed in along the spine daily until the gums are slightly but distinctly touched. Iodide of potassium, useless at this stage, may be of advantage when the condition becomes more chronic, when quinine, iron, and even strychnine may be called for. Where cold applications alone are not capable of subduing the pain, morphine should be freely given by subcutaneous injection; and, if the spasms be very severe, it may even be necessary to supplement the use of this drug by inhalations of chloroform. Belladonna or atropine has been found useful in mild cases. Of hypnotics chloral hydrate has a high reputation, and may be given alone or in combination with bromide. The various other hypnotics, such as chloralamide, sulphonal, trional, veronal, or paraldehyde, are of use in different cases.

Sequels such as contractures and muscular atrophies call for massage, electrical, and other special treatments, according to the precise condition present.

**B. Cerebrospinal Meningitis** (see Vol. I. p. 923).

**C. Tuberculous Spinal Meningitis.**—This form of meningitis is exceedingly rare except in combination with a similar condition of the cerebral meninges (Vol. VIII.). Seitz found this combination in 12 out of 20 cases of tuberculous cerebral meningitis in the adult. The spinal affection is commonly met with when the meninges at the base of the brain are affected; indeed, according to Schultze, this is perhaps always the case. On the other hand, it seems possible that in some cases the affection of the spinal may precede that of the cerebral meninges.

*Morbid Anatomy.*—As in other forms of leptomeningitis the dura mater may be quite normal and free; whilst in other instances there is some inflammatory infiltration of this membrane; and it may be adherent in places to the arachnoid. The latter membrane is turbid-looking and thickened; its vessels share in the inflammatory process, their walls being infiltrated and thickened; and the subarachnoid space is filled with turbid fluid and fibrinous exudation. The pia mater is also very turbid-



looking and thickened, and extremely hyperaemic. Miliary tubercles may be distinctly seen, but they are not nearly so commonly found as in the cerebral pia. On microscopical examination this membrane is seen to be infiltrated with large numbers of round cells, and, as in the case of the arachnoid, the walls of the vessels are infiltrated.

As the condition is so often secondary to a basal tuberculous meningitis, although the process may be met with throughout the whole length of the spinal cord, it may be limited to the cervical and upper thoracic regions. On the other hand, strange as it may seem, little or no evidence of implication of the meninges of the upper end of the cord may be found, while distinct evidences of tuberculous deposits may be seen in the lumbo-sacral region. I once examined a case in which with a basal meningitis, itself secondary to a tuberculous tumour removed from the cerebellum by Sir Victor Horsley, the meninges of the upper cervical region shewed least sign of implication; whereas the pia-arachnoid throughout the whole extent of the remainder of the spinal cord was distinctly affected.

The morbid changes are limited, as a rule, to the meninges of the dorsal aspect of the spinal cord; occasionally, however, the ventral aspect is involved also. As in ordinary acute leptomeningitis, so here the nerve-roots and spinal cord may present evidences of secondary implication. The posterior roots are especially apt to suffer, round-celled infiltration occurring in connexion with the peri- and endo-neurium. The periphery of the spinal cord naturally suffers most, a marginal or peri-myelitis, as it has been called, being the result. The infiltration of the spinal cord takes place by certain definite routes, as by the septa of the pia which dip into its substance, by the marginal vessels which have a similar course, and by the entering posterior roots. The consequent changes in the cord may be very irregular and diffuse; the neuroglial fibres are swollen, and varying degrees of destruction of the nerve-elements are met with. Secondary degenerations naturally follow; but, in addition to this, there may be a degeneration in the posterior and lateral columns, in the ganglion-cells of the ventral horns, and in the ventral roots, which, according to Leyden and Goldscheider, is an affection of the neurons, comparable to, and indeed the central homologue of, the peripheral neuritis which occurs in tuberculosis.

*Symptoms.*—Clinically the spinal symptoms may be quite overshadowed by those due to the concomitant affection of the cerebral meninges. When present, such spinal symptoms differ in no way from those which result from other forms of affection of the spinal leptomeninges, and need not be repeated here.

Neuralgic pains, sciatica, and the like, occurring in tuberculous subjects, should place us on our guard; such symptoms may indicate the existence of tuberculous spinal meningitis.

It is not common for the spinal form of tuberculous meningitis to progress rapidly; as a rule, it runs a more or less subacute course. Indeed, in the majority of instances the limitation is determined by a



concomitant cerebral affection, which in some cases appears in point of time to be secondary to the spinal meningitis.

*Diagnosis.*—Of primary importance in the diagnosis of this variety of meningitis is the detection of tuberculous lesions in other organs of the body, notably in the lungs and pleurae. In the absence of such lesions there may be external evidences of scrofula; or the cachectic appearance of the patient may suggest the true nature of the condition. The detection of tubercles of the choroid on ophthalmoscopic examination would of course be conclusive; but, as a rule, this evidence is not forthcoming until the final stages of the disease.

This form of meningitis is especially apt to be confounded with the syphilitic; but in the latter, besides the importance of the history of infection, we have the results of the Wassermann reaction and of anti-syphilitic treatment to aid us; moreover, the motor disorder is much greater than in the tuberculous variety.

In order to establish a diagnosis between this condition and purulent meningitis we have to rely on the rate of development of the symptoms and the degree of pyrexia present; for, although in some slight cases of purulent meningitis there may be little or no fever, the condition is usually more severe, and attended with marked pyrexia. In tuberculous meningitis, on the other hand, fever is absent, or only slight, and the early stage of the affection is protracted.

It is in lumbar puncture, however, that we have the most certain means of diagnosing the nature of a spinal meningitis. The cerebro-spinal fluid withdrawn should be centrifuged, and cover-glass preparations made from the deposit and stained for leucocytes and tubercle bacilli. In the event of negative results inoculation experiments on guinea-pigs should be performed; for positive results are thus obtained when the examination of a large number of cover-glass preparations fails to detect the tubercle bacillus. The opsonic index may prove helpful where the other tests have left the diagnosis in doubt.

*Prognosis.*—The disease is nearly always fatal; even when it is apparently primarily spinal, the advance of cerebral symptoms may close the scene. It appears possible, however, for a circumscribed tuberculous spinal meningitis to end favourably, as in a case recorded by von Leube.

*Treatment.*—No measures hitherto adopted have been attended with the success claimed for lumbar puncture as a therapeutic measure. In view of the satisfactory results obtained from laparotomy in connexion with tuberculous peritonitis, it is possible that drainage and washing out of the subdural space, through one opening at the upper and another at the caudal end of the neural canal, may yield satisfactory results.

**D. Chronic Leptomeningitis.**—There can be no question that chronic changes in the pia-arachnoid, consisting in diffuse or circumscribed thickenings and cloudiness, are commonly met with on necropsy; but it is equally certain that in the great majority of such cases nothing in the clinical manifestations had pointed to meningitis.

Such a condition of the leptomeninges is met with in hypertrophic

cervical pachymeningitis, internal pachymeningitis haemorrhagica, and syphilitic spinal meningitis; or in diseases such as tabes dorsalis, general paralysis of the insane, myelitis, and tumours.

Moreover, it is none the less clear that formerly a clinical diagnosis of chronic meningitis was often made without justification. Cases of so-called spinal irritation, neurasthenia, and hysteria, in all of which pain and tenderness of the back may be prominent features, were commonly so regarded. Injuries, such as railway accidents and the like, which are frequently responsible for such functional disturbances of the nervous system, supplied no small number of cases of supposed chronic meningitis. But organic disease of the spinal cord has been also so regarded, a myelitis with meningitis being looked on as one of the latter condition alone; indeed, according to Sir W. Gowers, the clinical picture now regarded as characteristic of spastic paraplegia used to be always considered as a chronic meningitis. Making allowances for all these possible fallacies, two classes of cases still remain to be discussed: those in which the changes met with are the result of a former attack of acute meningitis, and those in which such thickenings are seen in the spinal leptomeninges of the subjects of chronic alcoholism and of senile degeneration. In the former class of cases some authors contend that such residual changes do not remain after acute meningitis, and that when recovery takes place from such an attack it is complete. With regard to the latter class of cases also, it has been argued, that though the condition of the meninges met with in chronic alcoholism and senile degeneration is regarded as inflammatory, there is no clinical evidence of this.

*Morbid Anatomy.*—A diffuse change of the leptomeninges may be met with throughout the greater part of the long axis of the spinal cord; but even when such is the case, the thickening is most pronounced on the dorsal aspect, and is most marked at the caudal extremity of the cord, becoming less and less so as higher levels are reached. It may be so great that the surface of the cord is to be seen with difficulty through the meninges. Apart from this general tendency for the change to be most pronounced at the caudal end of the cord, the thickening is not uniform, but is irregular in distribution. The inner surface of the dura mater is, as a rule, also cloudy, and presents similar irregular thickenings and nodular formations. The microscopical appearances vary with the age of the process; the proliferation of connective tissue may even shew but little fibrous structure, whilst with more fibrous structure evident the cell-elements may be still very scarce; in the earlier stages the cells are naturally more plentiful. The septa, which extend from the pia mater into the substance of the cord, are similarly thickened; and the margin of the cord may shew a varying degree of sclerosis, with a little secondary ascending and descending degeneration as a result of the slight damage done to the nerve-elements. Yet on the other hand, with chronic changes evident in the meninges, the interference with the spinal cord may not be sufficient to give rise to any recognisable secondary degenerations in it. The walls of the blood-vessels are thickened.

*Symptoms.*—I may repeat that, in the majority of instances in which this condition is met with, apart from any association with hypertrophic cervical pachymeningitis, internal pachymeningitis haemorrhagica, syphilitic spinal meningitis, caries of the spine, tumours, myelitis, and chronic degenerative diseases of the spinal cord, no clinical manifestations have been present which could be attributed to chronic leptomeningitis. Where symptoms exist they are indistinguishable from those resulting from chronic pachymeningitis, which have been fully dealt with already under that head. The affection runs a chronic course without febrile reaction. Pain and stiffness of the back are prominent features; lancinating pains may occur in the trunk and limbs, and pain on movement of the spine may be present; as also may tender points on pressure along the spine—hyperaesthesia of the skin and muscles. Moreover, if sufficient damage have been done to the nerve-roots, atrophic paralysis of limited extent may ensue, as may spastic changes in the legs when the spinal cord has been much interfered with. It is more than probable that many of the cases belong to the variety to be described next.

**E. Serous Spinal Meningitis.**—Sir V. Horsley has recently called attention, in this country, to this form of chronic meningitis, with which he has long been familiar, and the first published clinical record of which was made by Spiller, Musser, and Martin in 1903, five years after Schlesinger had described the condition anatomically. Krause and Oppenheim have also contributed to our knowledge of this form of meningitis, which is important if for no other reasons than that it is easily mistaken for tumour of the spinal cord, and lends itself to successful surgical treatment.

Nothing very definite is known as to the cause of the condition, which usually occurs in adults, except that syphilis and gonorrhoea have each been suspected, and that some of the cases may owe their origin to influenza. The lower half of the cord has been involved as a rule, and the symptoms have pointed to the mid-thoracic region as the highest level of implication in most instances. The theca is greatly distended by excess of cerebrospinal fluid, which may be so shut in within given limits as to warrant the term "circumscribed spinal meningitis," which has been applied to it by Spiller. The cord is thus compressed, and is usually shrunken in appearance.

Little need be said of the *symptoms*, except that they resemble those of a tumour compressing the cord. It follows that the patients experience pain with loss of power in the lower limbs, and that, unless relieved by operation, progressive paraplegia results in death.

*Diagnosis.*—The points on which Sir V. Horsley lays most stress as distinguishing these cases from cases of tumour of the cord, are the more diffuse character of the pain, the uniform loss of power in a limb without any limitation of the paralysis to a group of muscles supplied by a single nerve-root, and the absence of vasomotor and trophic phenomena such as commonly obtain in compression-paraplegia, the result of caries or tumour.



The *prognosis* is good in people who have not passed the middle period of life, if operation is not too long delayed.

The *treatment* recommended by Sir V. Horsley is laminectomy followed by opening the theca and washing out with mercurial lotion.

III. TUMOURS OF THE SPINAL MENINGES.—No detailed description of tumours of the spinal meninges, and the effects to which they give rise, is called for here, as they are dealt with in the special article on "Tumours of the Spinal Cord" (p. 868).

IV. CALCIFICATION OF THE DURA AND ARACHNOID.—It is quite common to meet with this condition of the arachnoid, but it is very rare in the dura. In the arachnoid irregularly circular or oval shell-like plates of varying sizes, with scalloped margins, are seen; they are of an opaque white colour, and thicker in the centre than at the periphery. They are usually met with in the lower thoracic and lumbo-sacral regions of the cord; they are rare in the cervical region, and when they do occur in the latter situation only a small platelet here and there is usually seen, and larger and more numerous plates will generally be found also in the lower thoracic and lumbo-sacral regions of the cord. They occur most commonly, and in greatest numbers, on the dorsal aspect of the spinal cord; though they may also be met with on the ventral aspect.

It is not clear how these platelets originate; for, though a previous meningitis might account for them, there is little to support this suggestion, either from the evidence of the morbid anatomy or of the clinical history. In the majority of cases of the kind that I have examined, even where the platelets have been numerous, and some of them large, there has been a total absence of any other condition attributable to meningitis. There has been no adhesion of the dura to the arachnoid, and the latter membrane, with its contained platelets, has been freely movable over the subjacent pia mater. In only one instance were there concomitant signs of chronic meningitis present; these consisted in adhesion of the dura to the arachnoid over limited areas, and of patches of thickening and matting together of the arachnoid and pia in places. In none of the cases was there anything in the clinical history to point to a previous inflammation. Meningitis of any intensity is usually so stormy in its manifestations that it is difficult to believe that this condition of the meninges, if dependent on a former meningitis, could be met with so frequently without any such clinical evidence. It is, of course, possible that a meningitis, slight in degree and more or less subacute or chronic, may run a latent course; or give rise only to symptoms of so slight a character that little attention is paid to them; but any degree of exudation in such cases would be uncommon, whilst these platelets in their characters rather suggest the remains of such an exudation.

V. PIGMENTATION OF THE SPINAL ARACHNOID.—This condition,



first described by Valentin, has been very carefully studied by Virchow. It was formerly looked on as the remains of a previously existing hyperaemia, or inflammation of the membrane; but it has no pathological significance. In contradistinction to the condition last described, it is most common in the meninges of the cervical region, and on the ventral surface of the cord and medulla oblongata. Macroscopically the morbid change gives rise to a general slightly dark or black-grey tint, which on closer inspection is seen to depend upon collections of black or brown specks. On microscopical examination the change is seen to be due to the presence of pigment-cells similar to those of the choroid; they are spindle-shaped, or may be stellate, and possess a nucleus.

VI. HYDRORRHACHIS, or an excess of fluid in the arachnoid space, like the last condition, was formerly regarded as the result of venous congestion or inflammation of the meninges.

An excess of fluid is commonly met with in intracranial conditions associated with increase of the cerebrospinal fluid; such as external or internal hydrocephalus, the various forms of meningitis, including the tuberculous variety, cerebral tumour, and cerebral abscess. So too in diseases attended with general dropsy, the arachnoid sac may contain an excess of fluid. In conditions of this kind more especially, although excess of fluid probably existed in the sac during life, it is not unlikely that a considerable accession is made during the final moments which precede total dissolution.

Formerly a definite group of symptoms was supposed to result from the pressure on the spinal cord and occasioned by the excess of fluid in the arachnoid sac; but it is highly improbable that the fluid is ever present in sufficient amount to cause a degree of pressure capable of disturbing the functions of the spinal cord, unless the case be one of serous meningitis (see p. 617).

VII. VARICOSITY OF THE VEINS OF THE PIA MATER.—This condition does not call for any special description except that care should be taken not to mistake for it the fulness of vessels so commonly seen at necropsies, after the cadaver has been in the dorsal position during the interval between death and the time of the examination.

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## DISEASES OF THE SPINAL CORD

ACUTE POLIOMYELITIS.

MYELITIS.

LANDRY'S PARALYSIS.

HAEMATOMYELIA.

CAISSON DISEASE.

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MOTOR NEURON DISEASE.

BULBAR PALSIES.

SYPHILIS OF THE SPINAL CORD AND  
ITS MEMBRANES.

TABES DORSALIS.

FAMILIAL AND HEREDITARY ATAXIA.

SUBACUTE COMBINED DEGENERATION.

SENILE PARAPLEGIA.

DISSEMINATED SCLEROSIS.

SYRINGOMYELIA.

TUMOURS OF THE SPINAL CORD AND  
ITS MEMBRANES.





## ACUTE POLIOMYELITIS

SYNONYMS.—*Infantile spinal paralysis* ; *Regressive paralysis* ; *Acute atrophic paralysis* ; *Atrophic spinal paralysis*.

By M. ALLEN STARR, M.D., LL.D., Sc.D.

ANTERIOR poliomyelitis is an acute disease observed most commonly among children, but occasionally in adults, characterised by sudden complete loss of power in one or more limbs, followed by wasting of the muscles paralysed, and by interference with the growth of the parts, but not attended with any sensory disturbance. It occasionally occurs in epidemics, but sporadic cases are constantly observed.

Etiology.—Anterior poliomyelitis occurs with about equal frequency in the two sexes. Hereditary influences play no part in its causation. It is essentially a disease of infancy, although it occurs at all ages of life ; cases have been noted in adolescence, in adult life, and even in old age. The following table (Table I.) demonstrates that the

TABLE I.—Age of Onset in Anterior Poliomyelitis.

	Year.									
	1	2	3	4	5	6	7	8	9	10
Seeligmüller . . .	20	25	18	1	1	2	...	...	...	...
Galbraith . . .	17	38	15	4	1	...	...	...	...	...
Sinkler . . .	44	92	55	29	9	2	3	6	0	3
Gowers . . .	21	21	25	9	17	4	2	6	4	...
Starr . . .	29	76	61	30	20	9	5	2	5	3
Total . . .	131	252	174	73	48	17	10	14	9	6

majority of cases occur during the second and third years of life, and that the disease is rather rare after the age of six. It has been supposed by some authors that cases of congenital club-foot are due to the occurrence of anterior poliomyelitis in utero ; and it is certain that such cases are usually associated with a congenital lesion of the sacral region of the cord. This lesion, however, is usually due to a defect

of development rather than to a vascular disease; hence the assertion that anterior poliomyelitis may occur in utero is open to doubt. That the disease may occur very early in life is confirmed by the case recorded by Duchenne, in which the child was but twelve days old; and Sinkler has recorded a case in which the child was six weeks old. The youngest patient in my own records was two months old.

The season of the year appears to have a direct relation to the occurrence of infantile paralysis. W. H. Barlow called attention to this in his monograph in 1878, and it has been noticed by Sinkler in his numerous

TABLE II.—Month of Onset in Anterior Poliomyelitis.

	Barlow.	Sinkler.	Gowers.	Starr.	Lovett.
January . . . . .	1	14	1	5	8
February . . . . .	0	8	1	2	4
March . . . . .	4	11	1	9	5
April . . . . .	2	21	1	4	5
May . . . . .	4	21	1	5	6
June . . . . .	5	61	11	10	13
July . . . . .	16	109	13	42	36
August . . . . .	11	124	13	57	43
September . . . . .	4	79	15	41	47
October . . . . .	3	45	6	18	39
November . . . . .	1	12	2	6	29
December . . . . .	2	12	5	3	4
	53	517	70	202	239

papers. Sir W. Gowers also confirms the statement. Table II. shews the month of onset in the cases recorded by various authors. It will be noticed that the vast majority of the cases occur in June, July, August, and September; that is, during the months of greatest heat in England and in America.

The fact that this disease has occurred in epidemic form has thrown considerable light upon the etiology; and has made it extremely probable that it should be regarded, at least in some cases, as an acute infectious disease. Colmer was the first to record the occurrence of the disease in epidemic form; for, in describing a case of this kind, he noted that the parents of the child remarked that in their village eight or ten other children had been attacked with similar symptoms within three months.

Cordier, in the months of June and July 1885, saw 13 cases of infantile paralysis in the town of Sainte Foye l'Argentière, a town with a population of 1500 persons, where in other years the disease had been extremely rare. In 1890 Leegaard reported that in the little village of Mundal in Norway 8 cases of infantile paralysis had been seen between the last of July and the first of September, the disease never having been seen in the town before. Medin of Stockholm also describes an epidemic of the disease in Sweden (18). In 1888 he saw during the

spring 5 cases; and between the 1st of August and the 1st of November 44 cases had been observed. Necropsies were made in some of these cases which proved the disease to be a pure anterior poliomyelitis. In Umea in 1881 Bergenholtz observed a small epidemic of 13 cases. An extensive epidemic of the disease was observed by Caverly in 1895 in Rutland, Vermont. Through his courtesy I examined a number of his cases during this epidemic. The epidemic occurred between the 20th of July and the 20th of September. 140 cases of the disease occurred, of all grades of severity; and, though they appeared chiefly in infants and children, adults were not exempt. Pieraccini observed 7 cases occurring within a few weeks in July and August 1895 in a small village near Florence (Italy), where at that time an epidemic of whooping-cough was prevailing. In 1896 an epidemic occurred in Port Lincoln, South Australia, and in 1904 there was a severe epidemic in Sydney. An extensive epidemic occurred in Sweden and Norway in 1905, which was carefully studied by Wickman and by Geirsvold, 1500 cases being observed. The most extensive epidemic known occurred in New York in 1907 when over 2000 cases developed during the summer (24). In 1908 epidemics occurred in Vienna (Zappert), in Victoria (Stephens), and a small one at Upminster (Treves). In most of these epidemics the mortality varied from 6 to 10 per cent, a point of importance, as death is rare in sporadic cases. Death usually occurred on the fourth or sixth day of the disease from respiratory paralysis. Many abortive cases with complete recovery were also observed. In the Swedish and New York epidemics careful studies of the blood and of the cerebrospinal fluid failed to reveal the presence of any micro-organism, and no serum-reaction could be demonstrated. There is some evidence of contagion in these epidemics; in several cases children contracted the disease after moving into tenements where other children had died of the affection. It has been shewn experimentally by Flexner and Lewis (1910) that the virus of epidemic poliomyelitis is eliminated by the nasopharyngeal mucosa.

Another indication of the infectious origin of infantile paralysis is its frequent occurrence in connexion with other infectious diseases, or subsequent to them. Among my own cases, diphtheria, meningitis, measles, pneumonia, scarlet fever, and acute malarial poisoning were noted as having occurred in a number of cases just before the onset of the disease. Sir W. Gowers, it is true, questions the relation between its occurrence and that of other acute febrile diseases, but the coincidence has been observed by too many different authors to be merely accidental.

Exposure to cold or to sudden check of perspiration has been alleged as a proximate cause. I have seen several cases which have arisen in boys after swimming in very cold water, and it is not unlikely that the frequency of its appearance in summer is due to occasional chill. Trauma has also been regarded an immediate cause, and in several recorded cases children have been paralysed after a fall or a blow on the back (1). Inasmuch as vascular disturbances are at the basis of the

affection in many cases, there is every reason to believe that trauma may be a causal factor. Whether the functional hyperaemia consequent upon the increased activity in the lumbar region of the cord at a time of life when the child is learning to walk may account for the frequent occurrence of paralysis in the legs at that time, is an open question ; but if haemorrhage or thrombosis of the spinal vessels be accepted as the fundamental pathological condition in the non-febrile cases this factor cannot be disregarded.

**Morbid Anatomy.**—The pathological change at the root of anterior poliomyelitis was first investigated by Cornil and Chareot. The specimens which they described were, however, obtained from chronic cases long after the onset of the disease ; hence their description, while still valid for such older cases, does not represent the pathological process in its early stage. More recent necropsies obtained by various observers—among whom Drummond, Rissler, Goldscheider, Dauber, Redlich, Siemerling, and Trevelyan may be mentioned—upon cases which ended in death within a week or ten days, or a few months of the onset, have shewn the following appearances :—

The spinal meninges are congested, and here and there haemorrhages of small extent are found in the dura and pia mater. In the epidemic cases an exudation of cells in the meninges has been found, and in the rapidly fatal cases the evidences of a complicating meningitis. The external appearance of the spinal cord is unchanged, but upon section the anterior portion of the grey matter, and frequently the central and posterior portions to a less extent, are found softened, so that they swell up above the cut surface, and are markedly red, with here and there small haemorrhages and distended vessels. These changes are in some cases limited to one anterior horn ; in some cases they extend through one entire enlargement of the cord ; in others they are found in both enlargements, or even throughout the cord. These changes are sometimes more extensively disseminated than might be supposed from the clinical history of the case.

On *microscopical examination* there is found a marked hyperaemia of the tissue ; all the blood-vessels are engorged and surrounded by exudation alike of serum, of leucocytes, and of small cells. The serum fills the lymph-spaces about the vessels and about the nerve-cells. The leucocytes infiltrate the tissues about the cells, cluster around the cells, and make their way into the cells. There is a great increase of small cells and nuclei in the neuroglia, which may be due to proliferation of the neuroglial cells or of the endothelial elements, or may be due to an emigration from the blood-vessels. This infiltration of the tissues with leucocytes and nuclei may be so intense as to obscure all other elements. Ruptured capillaries and small haemorrhages are seen here and there. It is thus evident that the supporting substance (neuroglia) of the grey matter and the blood-vessels are involved in the inflammatory process.

The changes in the ganglion-cells (motor neurons) of the cord are equally characteristic. These cells shew great varieties of degenerative changes depending partly upon the severity of the case and partly upon



the length of time the process has been going on in any one cell. The earliest change in the cell is the cloudy appearance of its protoplasm—an increased granular appearance obscuring the nucleus and leading to its deeper staining by the reagents. The chromophil granules when stained by the Nissl method seem larger than in normal cells, and the nucleus appears to be granular. In the next stage of degeneration the protoplasm absorbs stains no longer; the chromophil granules lose their typical arrangement about the nucleus; the nucleus is faint and the cell has lost its sharp outline, and some of its prolongations. Later still the cell appears changed into a swollen, shapeless, or spherical ball of matter, and its protoplasm is altered into a homogeneous unstained mass with vacuoles, or has become distinctly granular, in which case it stains deeply. At this stage the prolongations are entirely absent. The last state is one of shrinkage, the cell-body being changed into a small deeply stained mass hardly larger than its original nucleus. During the later stages leucocytes penetrate into the pericellular space and encroach upon the cell-body. In the nerve-fibres, and in both the protoplasmic prolongations and neuraxon of the cells, similar processes of degeneration are found until a complete destruction of all the processes of the cell is brought about. During the first two stages of this process of inflammation in the cell an arrest may occur and repair be established; but the cells which have lost their processes are permanently damaged, and fall into atrophy.

The change in the interstitial tissue and in the ganglion-cells is not in all cases parallel in degree. Some cases have been observed in which the cellular degeneration was attended by few or no changes in the vessels and interstitial tissue. If the case be examined some weeks or months after the onset, the vascular changes are no longer evident; the serous exudation has been absorbed; there are no longer leucocytes and cells within the interstitial tissues, wherein only an atrophied rarefied neuroglia is left, containing a few normal cells and many nuclei, the relics of degenerated cells. In some parts the anterior horn may be changed even into true sclerotic tissue; and here and there a small cavity may be found within the sclerotic mass. In some cases the apparent change in the basis substance and neuroglia is very slight, and the only change is an atrophy of the ganglion-cells, such as Charcot described. The degree in which various groups of cells are affected varies greatly at different levels or even at the same level; so that some groups appear to be affected whilst others escape.

The result of this atrophy of the cells and surrounding tissue is a gradual shrinking in the entire size of the anterior horn; and as the nerve-fibres arising from these cells pass into the anterior and antero-lateral columns, and into the anterior spinal nerves, there is an accompanying atrophy in these columns and in these nerves. Many of the cells in the anterior horn are association-cells with neuraxons which pass only to other levels of the cord through the antero-lateral columns; and these also suffer in the lesion. Hence in cords examined late in the

disease there is a manifest deformity of the entire enlargement affected, and on section decided shrinkage and apparent sclerosis of the columns around the anterior horn are seen.

Considerable discussion has arisen on the exact origin of this inflammatory process, and two opposing hypotheses are current regarding it. The majority of recent observers believe that in anterior poliomyelitis we have an acute inflammatory process, similar to that in general myelitis but limited to the domain of the anterior spinal arteries; and that the atrophy of the spinal cells is the terminal stage of this process of general inflammation.

According to a few observers (von Kahliden) there are cases in which the disease is a degeneration limited exclusively to the anterior cells, and not accompanied by any general inflammatory process; and these observers still maintain that the original description of Charcot is correct.

A haemorrhage into the anterior horn, or a thrombosis of one of the branches of the anterior spinal artery, has been supposed to be the lesion in the cases which begin suddenly without fever; but although this hypothesis is likely enough, no actual observations can be found to support it. It has been shewn by Sir C. Allbutt and others that slight haemorrhages occur in the spinal cord in children, either spontaneously or after slight injuries. The exact pathology of these cases is still unknown.

As a consequence of the spinal lesion there is a degeneration and atrophy of the anterior nerve-roots and of the motor fibres in the nerves of the body proceeding from the segment affected by the lesion. There is also a granular degeneration of the muscle-fibres in the early stage; and finally the muscles are changed into fibrous bands, infiltrated in some cases with fat. Mention must also be made of the smaller size of the bones in the affected limb. This is rather an arrest of growth than a pathological state. Occasionally a true multiple neuritis is associated with poliomyelitis (17), both being due to the same cause.

**Pathology.**—The question of the bacterial origin of this disease has excited the greatest interest in recent years. Authorities are not as yet agreed on this question. A number of years ago Schultze described a case of anterior poliomyelitis in which he had found a diplococcus in the cerebrospinal fluid, and in isolated cases here and there this has been confirmed. In the epidemic in Norway reported by Geirsvold a diplococcus was observed in a number of the cases. On the basis of 17 cases examined in this epidemic, Harbitz and Scheel described infiltration of the spinal pia with lymphocytes, more marked on the anterior surface of the cord and following the sheath of the central arteries and veins; very well marked hyperaemia, oedema, and exudation within the spinal cord and a marked cell-infiltration in the grey matter of the anterior horns. They describe the infiltration of the vessel-walls in the white substance with lymphocytes and a typical degeneration of the ganglion-cells, but only in a few cases was there

any evidence of the presence of micrococci. These were of the nature of diplococci, but were not uniformly found. In the careful necropsies made by Wickman in the Swedish epidemic the same conditions were observed, and here again bacteria were not uniformly present. In eight necropsies careful cultures were taken; in four the result was negative, in one *Staphylococcus albus* was found, and in the three others *S. aureus* was discovered. These were considered as accidental infections of the test-tubes and not as causative agents of the disease. In 1909 Landsteiner and Popper produced paralysis in monkeys by inoculating the peritoneum with the spinal cord of fatal human cases. Flexner and Lewis conveyed the disease to monkeys by inoculation, into the brain and subcutaneous tissues, of an emulsion from fatal cases in man, and further transferred the disease through a series of monkeys. Römer obtained very similar results. Flexner and Lewis, and Landsteiner and Levaditi independently concluded that the infective agent of epidemic poliomyelitis belongs to the group of filterable and ultramicroscopic viruses.

**Symptoms.**—It usually begins like an acute infectious disease with fever, sometimes attended by convulsions, especially in infants; sometimes by considerable pain in the back, body, and limbs; sometimes by digestive disturbances, vomiting and diarrhoea; sometimes merely by general malaise. The temperature rises rapidly to 102° or 103° F., and the patient may have a chill followed by sweating. Sometimes the onset is very severe, the child is delirious and stuporous, and the head and back may be retracted, and the control of the sphincters may be lost. Such cases have been usually observed during the epidemics of the disease, and are rare in the sporadic form. The temperature remains about 101° or 102° F. for several days, with slight morning remissions, then gradually sinks to normal, the entire febrile movement rarely lasting more than a week. Within a day or two of the onset paralysis sets in, usually in both legs, or in both arms, or in one limb alone, or in all four extremities. If the child be young, and confined to bed by the fever, the paralysis may not be noticed until the second or third day. In older children and adults the paralysis is usually manifest within twenty-four hours of the onset. It is generally observed that children cry a good deal during the period of onset, and some of those who are able to complain say that they suffer from pain in the back and in the affected limbs. The pain may remain for some weeks. Occasionally there is some rigidity of the spine or neck suggestive of meningitis, but this soon subsides. There is no disturbance of the bladder or rectum, though rarely retention of urine has been noticed for a few days. There is no tendency to bed-sores or to trophic changes in the skin. There is no complaint of numbness or of paraesthesia, and there is never any loss of sensation; but the limbs are sometimes painful upon any movement, especially in the joints.

After the fever, with its attendant malaise and digestive disturbances, has subsided, and the general health has been restored, there remains a



paralysis more or less extensive. This paralysis is usually more widespread at the onset than it is destined to be permanently. Thus the child may at first be completely helpless, and later recover power in all but one limb; or the trunk may be paralysed at the onset, but not permanently affected. Both legs are commonly affected together, but the final paralysis is found in one limb only. Occasionally the neck muscles are distinctly weak, and there may be difficulty in swallowing. This is seen in cases in which the arms are paralysed, and yet the final paralysis may affect one arm only. The face has been paralysed with the arms, and the ocular muscles also, but these are rare occurrences. In a number of cases in which the final paralysis was limited to two or three muscles the original paralysis was widespread, involving all the limbs. In giving a prognosis in the early stage this fact should be remembered. Sometimes the onset of the paralysis is not sudden, but there is a gradual increase during a week or ten days, then a stationary period, and then a regression. The subsidence of the paralysis begins from a week to two months after the onset, and then goes on steadily; but it is not until after the lapse of three months that it is possible to determine what muscles will eventually recover. There is always a certain amount of permanent paralysis.

The muscles which are paralysed undergo atrophy, which is more rapid and complete in those that are to be permanently paralysed; and the change in the size of the limbs is well marked within a month. The paralysed muscles are relaxed, never rigid; and to the electrical tests they shew a reaction of degeneration. The reaction of degeneration consists in a loss of response of both muscle and nerve to faradic stimulus. The galvanic reaction of the muscle remains, but the normal contractility of such a muscle to galvanic currents is altered. For the first few months the muscle responds too strongly to galvanism, and contracts under the positive pole more quickly than under the negative pole (Vol. I. p. 456). Later, the contractility to galvanism progressively decreases until, in a totally paralysed muscle, it is lost. The muscles in which the faradic reaction is preserved, though paralysed for a time, will recover (*vide* p. 640). These muscles also preserve their tone, so that they contract when sharply percussed with a hammer.

The circulation is considerably impaired in the affected limb, which is cold, blue, and flabby, but not oedematous. In some cases the bone is subsequently hampered in its growth, so that in after-life the limb is shorter and more slender than its fellow.

Whilst the description just given of an acute onset with fever applies to about three-quarters of the cases of acute poliomyelitis, there remains one quarter in which there is no febrile onset. Of 100 consecutive cases in my clinic, 69 began with fever, and 31 began without fever. Sinkler reports 178 with fever, 40 without fever. In these cases the child, while in a state of perfect health, is suddenly paralysed in one or more limbs. It gives no sign of pain, it does not appear to be ill, and the paralysis surprises the mother by its sudden onset. In these cases the paralysis is soon followed by atrophy and by vasomotor paralysis.



It is not attended with pain or tenderness on motion, and usually decreases to some extent, leaving the limb, however, in part permanently paralysed. These two modes of onset of the disease are evidently quite distinct, and their pathological basis is probably different.



FIG. 77.—Paralysis and atrophy of the right leg due to anterior poliomyelitis. The imperfect growth, six years after the onset, and the secondary talipes are evident.

After the onset is over there is a slow progressive improvement up to a certain point, when the permanent condition of paralysis is found to vary greatly in different cases. Its situation is usually in the legs, and here two types of the disease may be recognised—the leg type and the thigh type. In the leg type the peronei, alone or with the anterior tibial

muscles, are most commonly affected, although the posterior tibial group may share in the paralysis, or, indeed, may be as fully paralysed as the others. As the paralysis persists, deformities of the ankle and foot will



FIG. 78.—Paralysis and atrophy of the right leg due to anterior poliomyelitis. The secondary curvature of the spine due to the shortness of the paralysed limb is well shewn.

appear, the form of subsequent talipes depending upon the muscles chiefly paralysed. In the thigh type the psoas and iliacus muscles and the glutei and muscles about the thigh are those chiefly affected; the muscles on the inner side of the thigh and the muscles below the knee often escape. In these cases the leg hangs like a flail from the body, and cannot support

the weight at all. In some cases nearly all of the muscles of the lower extremity are paralysed, and the atrophy is uniform throughout the limb. In these severe cases it is not uncommon for the muscles of the back and abdomen to share in the paralysis and atrophy. Figs. 77 and 78 shew the appearance of limbs paralysed and atrophic; Fig. 77 shews a



FIG. 79.—Paralysis and atrophy of the left arm and hand due to anterior poliomyelitis. The partial dislocation of the head of the humerus due to deltoid paralysis, and the abnormal abduction of the thumb, are evident.

secondary talipes, and Fig. 78 shews a secondary lateral curvature of the spine due to the shortening of the leg.

When the arms are invaded two types of paralysis have been described, the upper-arm type and the lower-arm type. In the upper-arm type the muscles about the scapula, the deltoid, the biceps and supinator longus, are paralysed and atrophic, and consequently the motions of the shoulder-

and elbow-joints are seriously hampered. In these cases the shoulder-joint is unduly movable, and the head of the humerus falls out of the socket. In the lower-arm type the muscles below the elbow are invaded; the flexors or extensors of the wrist and fingers, or both together, are affected, the supinator longus escaping. In other cases the interosseous muscles of the hand and the thenar and hypothenar muscles are paralysed, while the long flexors and extensors escape. Occasionally a combination of upper- and lower-arm types occurs, in which the whole limb is useless. Fig. 79 shews a case of total paralysis of the arm, with atrophy and falling of the head of the humerus out of its socket in consequence of the paralysis of the deltoid. The claw-hand is also present. The upper part of the trunk is occasionally involved in the paralysis, together with the arms. Rarely the muscles of the back and trunk only are permanently paralysed.

In a very few cases the entire muscular system of the body appears to be affected by this disease; both legs, the trunk, and both arms are more or less paralysed; yet even in these cases a careful examination will shew that the degree of the paralysis and atrophy is not the same in all the muscles. The relative frequency of paralysis in different parts of the body is shewn in the following table:—

TABLE III.—Distribution of Permanent Paralysis in Anterior Poliomyelitis.

	Duchenne.	Seeligmüller.	Sinkler.	Starr.	Total.
Both legs . . . . .	9	14	107	54	184
Right leg . . . . .	25	15	68	31	134
Left leg . . . . .	7	27	62	37	133
Right arm . . . . .	5	9	5	11	30
Left arm . . . . .	5	4	8	6	23
Both arms . . . . .	2	1	1	5	9
All extremities . . . . .	5	2	35	9	51
Arm and leg, same side . . . . .	1	2	26	9	38
Arm and leg, opposite sides . . . . .	2	1	1	6	10
Trunk . . . . .	1	...	22	4	27
Three extremities . . . . .	...	...	10	5	15

Occasionally the nuclei of the cranial nerves are invaded by the disease. Then strabismus, facial palsy, and paralysis of the tongue, larynx, and pharynx are observed. This is more frequent in the epidemic type.

In addition to the paralysis and atrophy there is in every case a loss of reflex action at the level of the lesion. The skin reflexes usually return after a time; but the deep reflexes are absent for a long period, even when a partial recovery of the muscle involved has taken place. Thus, the knee-jerk is uniformly absent when the thigh muscles are paralysed, and the elbow- and wrist-jerks when the arms are affected.

Sensation is preserved in almost every case; but I have so frequently observed a permanent hypersensitiveness to painful impressions in the



paralysed limb, that I cannot but believe that the lesion in the grey matter affects the pain-sense tracts in their passage through the cord at the level of their entrance, and has a relation to this symptom. There is a marked vasomotor paralysis producing a permanent lowering of the surface temperature and a lack of vasomotor response in the limb to applications of heat and cold.

Deformities of the joints are a common sequel in infantile spinal paralysis. The approximation of articular surfaces in health is secured in part by the tonic action of the muscles, especially at the shoulder, hip, and knee; hence paralysis of the muscles controlling these joints is attended by relaxation and a greater degree of mobility than normal. Thus, when the deltoid is paralysed, the head of the humerus falls from its socket, as shewn in Fig. 79; and abnormal extension of the knee is often seen in the upper-leg type of palsy. After some months of paralysis the muscles which are the natural opponents of the paralysed muscles are apt to become permanently contracted, and this condition also brings about deformities. In the case of the foot the action of gravitation on a flaccid part of the limb combines with the contracture to increase the deformity there; hence any of the forms of talipes may ensue on infantile paralysis (see Fig. 77). Similar deformities of the wrist are also observed, but these are not common. Curvature of the spine, from paralysis of the muscles of the back, is frequently seen, all the varieties of this change having been described (see Fig. 78). They differ from those due to bone disease in that they do not persist during suspension of the body by the head and arms. One of the most important points in treatment is to prevent the establishment of these deformities.

The progress of the disease in any case may be divided into stages. After an acute onset there is a stage of maximum intensity, lasting from one to six weeks, and followed by a period of steady improvement, which may extend from six months to a year. Then follows the permanent chronic condition in which the normal growth of the child may lead to a slow development of the limb, but not to any change in its power of use. It is very rare for a complete recovery to take place after an attack of infantile paralysis. Even in the slightest cases there is usually some weakness, slight atrophy, and coldness left; and one or two muscles will be particularly feeble. In the majority of cases considerable permanent paralysis remains, requiring the use of apparatus to assist the use of the limb and to prevent deformities. Death has occasionally occurred during the acute onset (Pirie), but is very rare; and, once this stage is passed, there is nothing in the disease to threaten life.

It is the chief characteristic of the atrophic paralysis in this disease that it selects certain muscles to the exclusion of others. This selection bears no relation to the arrangement of muscles in the limb, or to the conjoint action of muscles in producing any definite movement. It is wholly dependent upon the arrangement of the groups of cells controlling the different muscles in the anterior horns of the spinal cord.

In order, therefore, to understand the symptoms of the disease a

short consideration of the motor elements of the cord is necessary. The neurons which preside over the motion and nutrition of the muscles lie in the anterior horns of the spinal cord. They are not scattered irregularly through these horns, but they are grouped together in definite clusters. A series of sections of the cord made from above downwards demonstrates that the number of these groups varies in different segments of the cord; there being a large number of such groups in the cervical and lumbar enlargements, and fewer in the dorsal and upper cervical regions.

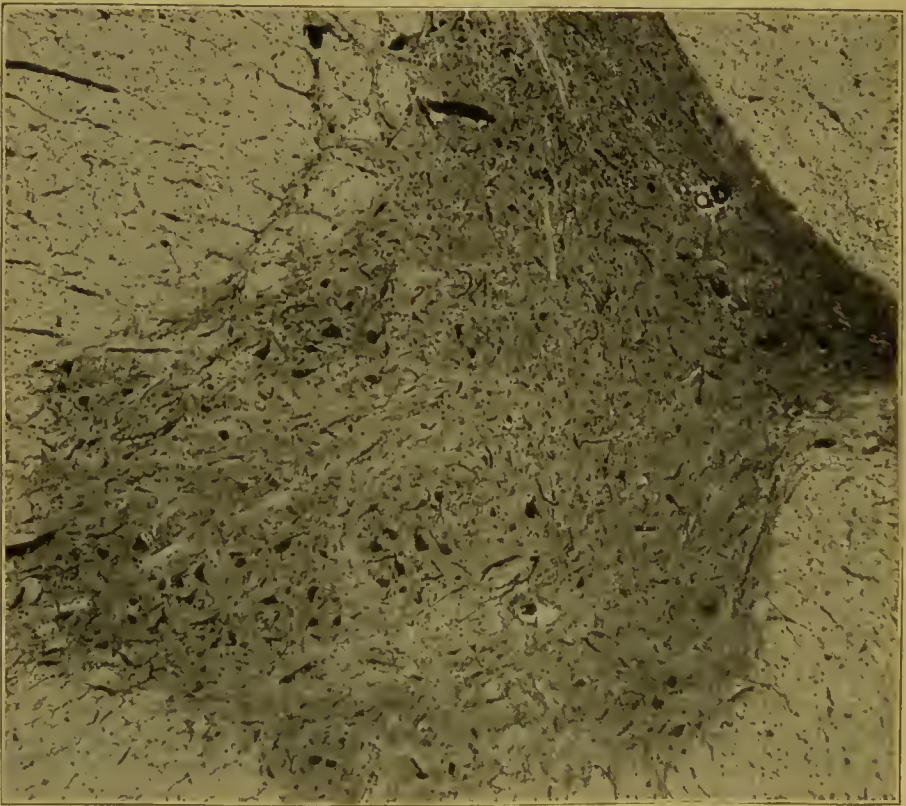


FIG. 80.—Section through the sixth cervical segment of a normal cord, shewing six groups of cells in the anterior horn.

Figs. 80 and 81 demonstrate this grouping of cells in the cervical and lumbar regions. Some groups of cells are very long, extending through three or four segments, whilst others are short, hardly reaching through one entire segment. It is evident that a lesion limited to a single segment of the cord may entirely destroy a group of cells limited to that segment, and may destroy only in part a column of cells extending into adjacent segments. If each group of cells represents a muscle, it becomes evident at once that the degree of paralysis in that muscle will be determined by the extent of the lesion in its group of cells. If a group of cells is entirely destroyed, its muscle will be totally and permanently paralysed. If a



group of cells is but slightly affected, the muscle may be weakened and slightly shrunken, but still able to perform its work. The following table, prepared by a careful comparison of a very large number of cases with accurate necropsies, shews the situation of the various groups of cells controlling the various muscles of the body in the different segments

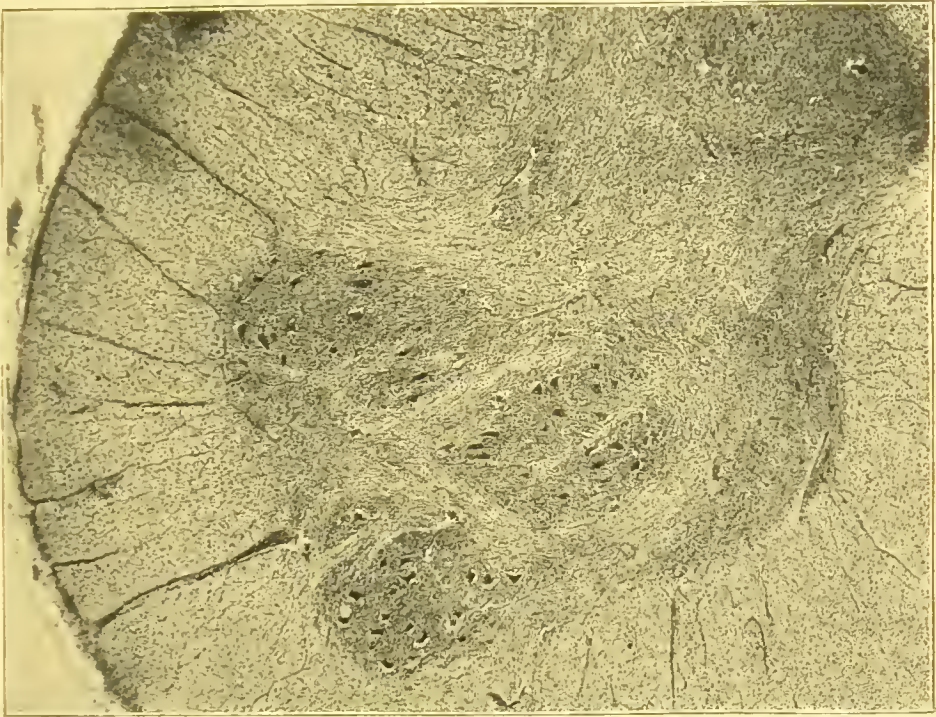


FIG. 81.—Section through the fourth lumbar segment of a normal cord, shewing three large groups of cells.

of the spinal cord (Table IV.). It will be seen that some muscles are represented in two or even three segments of the cord, whilst other muscles are represented in but one segment alone; and again it will be

TABLE IV.—Muscles represented in the Segments of the Cervical Enlargement.

4 C.	5 C.	6 C.	7 C.	8 C, 1 D.
Diaphragm. Lev. ang. scap. Rhomboid. Supraspin. Infraspin. Deltoid.	Supin. brevis. Teres minor. Rhomboid. Supraspin. } Infraspin. } Deltoid.	Pronators. Triceps. Brach. ant. Long extensors of wrist. ...	Pronators. Triceps. Brach. ant. Long extensors of fingers. Pector. (costal).	Extensors of thumb. Intrinsic muscles of hand.
Supin. long. Biceps.	Supin. long. Biceps. Serratus magnus. Pector. (clav.).	... Biceps. Serratus magnus. Pector. (clav.).	Latis. dorsi. Teres major. Long flexors of wrist.	Long flexors of fingers.

## Muscles represented in the Segments of the Lumbar Region.

1 L.	2 L.	3 L.	4 L.	5 L.
Quadr. lumb. Obliqui. Transversalis. Psoas. Iliacus.	Sartorius. Quad. ext. cruris. Obturator. Psoas. Iliacus.	... Quad. ext. cruris. Obturator. Adductores.	Glutei. Tibialis ant. (?) ... Adductores.	Glutei. Biceps femoris. Semi-tendin. Popliteus.

## Muscles represented in the Segments of the Sacral Region.

1 S.	2 S.	3 S.	4 and 5 S.
Biceps fem. Semi-membran. Ext. long. dig. Gastrocnemii.  Tibialis post.	Tibialis anticus (?). Peronei. Intrinsic muscles of foot. Gastrocnemii.  Tibialis post.	... ... Peronei. Intrinsic muscles of foot.	Sphincter ani et vesicae. Perineal muscles.

seen that different muscles are represented side by side in the same segment. If to this table the clinical picture of infantile paralysis be referred, it will become manifest at once that the distribution of the paralysis and the situation of the lesion bear a definite relation to one another. Thus it is evident that the upper-arm type of paralysis is produced by a lesion of the fifth and sixth cervical segments; that the forearm type of paralysis is produced by a lesion of the seventh and eighth cervical and first dorsal segments. It is evident again that the thigh type of paralysis is produced by a lesion of the upper lumbar segments, and that the leg type of paralysis is produced by the lesion of the lower lumbar and sacral segments.

The larger the extent of the lesion in the cord, the greater the number of muscles that will be paralysed. The more complete the destruction of the group of cells, the greater will be the degree of paralysis in the muscle. The greater the degree of paralysis in any muscle, the greater will be the degree of atrophy in the fibres of that muscle; so that any degree from slight to complete atrophy is possible. Inasmuch as the motor nerve to the muscle is merely a part of the motor cell in the cord it will be destroyed with its cell; hence an atrophy of the motor fibres in their passage through the antero-lateral column of the cord, and in the anterior root of the nerve, and in the nerve-trunk, to the muscle, is a part of the lesion of this disease.

**Diagnosis.**—There is no difficulty in recognising the disease; indeed, it is hardly likely to be mistaken for anything else. Occasionally a child attacked with acute articular rheumatism is unwilling, on account of the



pain in the joints, to move the limbs, and thus may be thought to be paralysed. A careful examination will soon demonstrate the true condition; for acute rheumatism never causes any atrophy or paralysis, and the local tenderness in the joints, the sweating, and the lack of coldness of the limbs may also aid in the diagnosis. Rickets may appear with a sudden febrile onset, and much pain and tenderness in the limbs and unwillingness to move. But the child is not really paralysed; and the state of its bones, the general condition and the sweating, as well as the lack of limitation of the pain and immobility to one or two limbs will prevent this disease from being mistaken for infantile paralysis. In some cases of acute poliomyelitis considerable pain is felt in the limbs, and some tenderness of the surface and of the muscles. The existence of pain during the first two days of the disease occasionally leads to mistakes in diagnosis. Thus, Marsh records the case of a child, five years of age, who was suddenly attacked with pain in the left leg extending down the thigh to the knee. The limb was flexed, abducted and rotated outward, and any movement was painful; hence the case was regarded as acute hip disease, but a closer examination shewed the hip-joint to be quite freely movable; and after two days, when the pain had passed away, the case was found to be one of infantile paralysis. The fever and general constitutional disturbances present at the onset had obscured the diagnosis. It has been suggested that when pain is severe, a neuritis accompanies the poliomyelitis. The existence of pain alone is not a sufficient reason to warrant this diagnosis, inasmuch as the more recent pathology indicates that in the early stages there is a congestion of the grey matter of the cord which might be sufficient to explain the pain. If, however, the pain continue, and tenderness come on in the muscles and nerves, it is probable that a neuritis due to the same infectious agent has set in. It is to be remembered that polyneuritis is usually a disease affecting the extremities symmetrically, and causing wrist-drop and foot-drop; that the distal parts are more severely paralysed than the proximal parts of the extremities; that there is no such selection of muscles paralysed as in poliomyelitis; and that there are usually sensory disturbances of a permanent nature—anaesthesia and analgesia or ataxia—in addition to the pain and tenderness along the nerves: hence in the stage of acute onset a polyneuritis should not be confounded with a poliomyelitis. When polyneuritis accompanies poliomyelitis, the clinical picture will be made up of a combination of these symptoms.

A localised neuritis of the brachial plexus (Erb's paralysis) causing paralysis of the deltoid, biceps, coraco-brachialis, and supinator longus is not uncommon in infants, and might be mistaken for infantile palsy. The history of injury during delivery and the local anaesthesia in the distribution of the circumflex nerve will, however, correct the mistake. Such cases usually end in recovery. For the diagnosis from amyotonia congenita see p. 23.

**Prognosis.**—The prognosis in anterior poliomyelitis is always grave. Patients do not often die of the affection, but they rarely escape a

permanent paralysis in some part of the body. It is true that in the majority of cases the original paralysis subsides, so that there is apparent improvement to a considerable degree. Thus, a patient who has originally been paralysed in both legs may entirely recover the power in one leg, and may be left with a condition of paralysis in the peronei or in the anterior tibial group of the other leg; so that the final condition is very much less severe than that at the onset. As a rule the limb that is affected never entirely regains its power, and usually shews some atrophy and shortening; the growth of a limb is hampered by the existence of the disease, and hence in a growing child the unaffected limb outgrows the other. It is thought that an electrical examination two or three weeks after the onset of the disease will afford some ground for a prognosis; that the muscles which respond to the faradic current three weeks after the onset of the disease will eventually recover, whilst those which fail to respond to this current at that time will always be somewhat impaired. The loss of faradic reaction, however, is not an indication that these muscles will be totally paralysed, since the faradic reaction has been known to return in a muscle a year after it has been lost; yet such a muscle never completely recovers its size or power. The prognosis is much better in the cases which begin with fever than in those which do not.

**Treatment.**—In the acute stage the treatment consists in keeping the child quiet in bed, and applying a mild form of counter-irritation along the spine; this is best done by a paste consisting of mustard one part and flour three parts, applied in a poultice along the back and removed as soon as the skin is reddened, and then again renewed; so that for at least a week there shall be continual counter-irritation without the discomfort of a blister; or dry-cupping along the spine may be applied frequently. Frequent sponging with alcohol and cool water is indicated in the cases in which the temperature is above  $101^{\circ}$  F., but phenacetin or antipyrin are not to be used unless the temperature reach  $103^{\circ}$  F. Harvey Cushing has proved that the administration of urotropin by the mouth results in the appearance of formaldehyde in the cerebrospinal fluid; and it can do no harm to give a child of three years old one grain of urotropin every six hours during the first ten days. A free purgation by a large dose of castor oil should be produced as soon as possible, some authors believing that the infection originates in the intestines, or that the disease is caused by a toxin produced there. There is some advantage to be gained from the internal use of ergot or of iodide of potassium in the early stage, and moderate doses of salicylate of strontium or of quinine may be used. If the child is in much pain or has convulsions, moderate doses of bromide, with or without codeia, may be employed as a symptomatic remedy. The general treatment of febrile conditions, a light diet, and laxatives should not be neglected. Rest in a prone position in bed is better than constant lying upon the back. Since it has been shewn by Flexner and Lewis (1910) that the virus of the epidemic poliomyelitis is eliminated by the nasopharyngeal mucosa, the secretions of the buccal and nasal cavities should be disinfected and destroyed.

When the acute stage has passed over, there is little to be done during the first week excepting to nourish the child well and keep the paralysed limb warm. Iodide of potassium in three to five grain doses may be administered three times a day.

When the paralysis begins to subside spontaneously it is well to administer strychnine in full doses— $\frac{1}{50}$  of a grain three times a day for a child of three years of age. This remedy is best given at intervals, not continuously; it is my rule to use it for a week and then intermit it for three days. The condition of mechanical irritability in unparalysed muscles, as determined by percussion with a hammer, is a good indication of the degree of the effect produced by the strychnine, and the strychnine may be increased up to a definite point of increase in this irritation. It is to be remembered, however, that twitching of the limbs and stiffness of the back, usually indicative of strychnine effects, are not to be expected in infantile paralysis where the muscles are paralysed. Whether general tonics, such as cod-liver oil, hypophosphites or arsenic, have any effect of a favourable kind may be left to the judgment of the physician in each individual case. The most important indication during the stage of regression is to preserve the nutrition and function of the paralysed muscles; and this is to be attained by skilful massage, by hydrotherapy, or by the use of electricity.

*Massage* is of the utmost importance in these cases and should be given once or twice a day with care, combined with such attempts at active movement as the child is able to make. Among the poorer classes it is well to instruct the mother how to do this, so that it should be given with persistence. The massage should not be of the hardest kind, and yet should be sufficient to stimulate the circulation in the limbs, and to promote the lymphatic and venous flow.

Next to massage *mechanical devices* which induce the child to make use of the weakened limb should be employed. A household gymnasium, adapted to the individual case, can easily be devised by the physician; and if such exercises are made a kind of play for the child, much good will be derived from his own efforts.

*Hydrotherapy* has also an important use. The general circulation in the cold and flabby limb is aided by warm baths, and it is my habit to order these children to play in warm water (temperature 98° F.) for half an hour twice daily. This warm bath may be followed by a cooler sponging and brisk rubbing, but cold water should not be employed for these children, as the temperature of the paralysed limb is always below that of health. Proper protection of palsied limbs by extra flannel clothing is always advisable.

*Electricity* is a valuable agent in the treatment of infantile paralysis, but a clear statement of its use should be made by the physician to the family. Electricity has no influence whatever upon the course of the disease. It does not affect the lesion in the spinal cord—either to decrease the hyperaemia, or to increase the nutrition of the nerve-centres. Applications of galvanism to the spine are therefore absolutely useless;



but applications to the muscles may be of distinct service in two different ways :—first, by causing their contraction, and thus exercising them when voluntary exercise is impossible ; and, secondly, by promoting those chemical changes in the muscle which are essential to growth and nutrition.

Examination of any case will reveal a certain number of muscles in the paralysed limb which respond to faradism. These muscles will eventually recover entirely, yet the tone and strength of the muscle should be kept up during the period of improvement by means of exercise with either the faradic or galvanic current. It is well proven that, as exercise of a healthy arm will markedly increase the size of the biceps muscle, so the application of faradism regularly to a susceptible muscle will increase the size of this muscle ; hence to the weakened muscles which still respond to faradism an application of the faradic current for about ten minutes once or twice a day will be of service. The majority of the paralysed muscles do not, however, respond to faradism, and it is time wasted to apply the faradic current to these muscles ; but they do respond, as a rule, to interrupted currents, the positive pole being placed over the muscle and the negative upon the limb at a short distance above. The interruptions should be made by an electrode held in the hand, and provided with a finger-key ; and each muscle should be treated for about three minutes daily—fifty to sixty interruptions a minute being made by the finger. The strength used should be the least which will secure contraction in the muscle. When interruptions of the current do not produce a prompt response, alternation of the current may be employed by reversing the current rapidly by means of the pole-changer on the battery. It is to be remembered that in this disease the application of electricity is more painful than in health. It is also to be remembered, in applying electricity to children, that their confidence must be gained ; if they are frightened at the first application subsequent treatment will be a continual struggle. It is my custom, therefore, to begin a course of electrical treatment to a child by several applications of the sponges and electrodes while no current is passing, thus accustoming the child to the apparatus and gaining its confidence. After two or three such applications a weak current may be used, and then day by day its strength may be increased, until by the end of ten days the necessary strength is attained. In this way a daily struggle, with unsatisfactory and probably useless applications, can be avoided, and the parents' consent obtained to a course of treatment to which they would eventually object if every application meant a struggle. Any intelligent mother or nurse can be taught to give the galvanism or faradism to a child in this manner, and it is best to interest the attendant in the treatment from the beginning, and to instruct her carefully, so that within a week the treatment can be left entirely in her hands. Such an application of electricity is to be made daily, or twice a day for two or three years. Spontaneous recovery will have reached its best at the end of the first year, but even after this time these muscles may be brought into a condition of hypertrophy by means



of continued exercise. When, however, a child is quite able with some force to move any paretic muscle, it is far better to rely upon voluntary exercises than upon electrical applications. If at the end of a year no effect is obtained in a muscle from massage, bathing, and electricity, there is no use in continuing the treatment of that muscle, as it will never recover; its nerve-cells are entirely destroyed.

The use of *mechanical apparatus* plays a great part in the treatment of infantile paralysis in the chronic stage. It is to be remembered that many weak muscles can do their work only when the limb is placed in an advantageous position, or when they are assisted in their action. Many of the muscles have, as part of their function, to keep the joints in place, and this part can be supplied by properly adjusted braces; hence an apparatus may enable the child to use a muscle or move a joint which it could not do if the joint were unsupported. Again, the result of paralysis of one group of muscles is to allow the joint to be bent by its opponent, or to yield to the influence of gravitation; hence, if a brace be not applied early to correct this tendency, the paralysis is often followed by deformity. There is no disease in which orthopaedic apparatus is of more service than in infantile paralysis, and it cannot be applied too early, as it may prevent the development of contractures and of deformities. There is no stage in which it is too late to fix a brace; for even when these deformities have occurred tenotomy may be employed to straiten and adjust a joint, and then the limb can be fixed by the brace in a proper position. But every case has to be treated skilfully in accordance with its own peculiarities, and the ready-made braces of the shops are often worse than none. A special apparatus for each case must be fitted under the direction of an orthopaedic surgeon; and it is to be remembered that in a growing child such apparatus must be constantly readjusted, its length and size being changed from month to month in accordance with the development of the limb.

In many cases of deformity, in which there is a strong contracture of a fairly healthy muscle overcoming the weak paralysed muscle, the question of *tenotomy* will arise. Tenotomy will of course result temporarily in a replacement of the deformed limb to its natural position; but, unless the joint can afterwards be held by a brace in a proper position, tenotomy alone will be of no permanent service. Hence, in some cases, tenotomy is only to be regarded as a preliminary to the proper application of apparatus. Apparatus has also been devised (especially in the treatment of infantile paralysis of the hands) by means of which weakened muscles may be reinforced by elastic bands so applied as to take the place of the paralysed muscle. Thus a drop-wrist or a paralysis of the extensors of one side of the wrist can be somewhat relieved by a series of elastic bands attached to the finger-tips, or to rings and to the elbow, and running through a bracelet at the wrist. Such devices, however, are usually discarded after a time, as they are more cumbersome than useful. Apparatus is especially applicable to spinal curvature of the paralytic kind; and in any case in which the body or back muscles are involved

at the onset, it is well for the child to wear a brace in order to prevent the establishment of some form of curvature.

A portion of the tendons of certain healthy muscles may be attached to the severed tendons of paralysed muscles about the ankle, knee, wrist, or elbow, in order that the healthy muscle may be made to do the work of the muscle which is paralysed. I have seen many cases in which the result was excellent, a portion of the tendon of the tibialis posticus being attached to the tendon of the peroneus longus, whereby all weakness and deformity were corrected. Periosteal implantation rather than tendon-grafting is preferred by some surgeons (Lovett and Lucas). An attempt has been made to restore power in paralysed muscles by grafting the central end of a divided normal nerve into the peripheral end of a divided atrophied nerve, care being taken to use a part only of the normal nerve in order to avoid the production of total paralysis in the muscles which it supplies. This method is still under trial. Lovett reports good results in 16 out of 20 cases.

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## MYELITIS

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MYELITIS in its strict etymological sense denotes disease of the spinal marrow, and in the history of medicine it has been used to embrace every kind of morbid process to which the spinal cord is liable. The general use of the suffix "-itis" for the purpose of suggesting inflammation, although it cannot be defended, has become so universal in medical terminology that it would seem desirable at first sight to reserve the name myelitis for the inflammatory diseases of the spinal cord. To this course there are serious objections, the consideration of which is of fundamental importance for the purpose of introducing and elucidating the modern conception of this disease. A brief account of the history of the disease will help to clear the ground, before entering upon this explanation.

The history of myelitis is essentially the record of a process of elimination which has been going on for a great many years, and which cannot even now be said to have reached its consummation. Ollivier used the name to cover almost all diseases of the spinal cord, and Landry, writing in 1853, raised the question whether there were any forms of paralysis independent of "la myélite."

The differentiation of systemic and other *scleroses* from the remaining myelopathies was largely due to the work of Lockhart Clarke, Gull, von Leyden, and Charcot, and the recognition of distinct forms of myelitis, to which the designations "transverse" and "acute central" were given, was a product of the same period. Although Dr Bastian pointed out in 1868 that cerebral softening was more often due to vascular disease than to inflammation, it was not until about fifteen years later that the possible thrombotic origin of spinal softening was seriously considered.

Since that time Oppenheim, Lancereaux, Marie, Dejerine, Bruns, Singer, and other observers have done much to advance our knowledge of this aspect of the question, with the result that a desire to separate the inflammatory from the vascular softenings of the spinal cord has found expression, and the adoption of such terms as "spinal thrombosis" and "myelomalacia" has been suggested. At the present time it is almost generally accepted that syphilis is an etiological factor in the majority of cases of so-called myelitis, and considerable controversy has arisen as to how far the preservation of this name in its widest sense is justifiable.

**Introduction.**—The result of an acute or subacute focal lesion of the spinal cord is a clinical picture which varies with the site more than with the nature of the morbid process. An accurate diagnosis of the latter



is often possible only after death, and not always then if the disease is of long standing. For this reason the term myelitis, whether inflammation or thrombosis forms the basis of the spinal lesion, is convenient from a clinical point of view, and by long usage has become the natural designation for cases of the kind.

It must be remembered, moreover, that thrombosis can never be regarded as the primary and sole factor in such cases. Thrombosis occurs as the result of disease of the blood-vessels, or as one of the phases of an inflammatory process. In the latter case the primary factor is of such a character as to justify the term myelitis. In the former the vascular disease may be either degenerative, as in some forms of arteriosclerosis, or, much more commonly, inflammatory, as in syphilitic arteritis. In the large majority of cases, therefore, the softening has some claims to be regarded as inflammatory in origin, and the difficulty of deciding in individual cases as to how far such claims can or cannot be substantiated is often insurmountable, at any rate at the bedside.

From the histological standpoint, too, the problem is frequently no more easy to solve. It may well be asked whether, even in recent cases, it is always possible to distinguish under the microscope between a purely thrombotic and an "inflammato-thrombotic" lesion. Some authors consider that in syphilitic thrombosis, although the larger vessels may shew perivascular cellular infiltration, yet the necrosed areas are free from cellular infiltration and from neuroglial proliferation; that in cases of simple inflammation, on the contrary, the excess of cells both in the perivascular lymphatics and in the surrounding tissues is an essential and striking feature. In reply to this it must be pointed out that there are instances of acute spinal syphilitic lesions in which thrombosis and consequent necrosis play a very insignificant part, and in which a gummatous infiltration of the tissues, rich in cells, provides all the appearances of an inflammation.

On the other hand, should the examination of the diseased cord be delayed, it is more than probable that the accurate discrimination between the inflammatory or vascular origin of the lesion will be impossible. Necrosis, sclerosis, and rarefaction of the tissues may be the results of either process, and the condition of the blood-vessels may not be sufficiently characteristic to justify a definite conclusion. Moreover, in some cases of spinal inflammation, not syphilitic in origin, areas of necrosis without cellular infiltration and independent of vascular thrombosis are met with and generally ascribed to toxic influence.

There are still two other points which cannot be overlooked in discussing the nomenclature of spinal softenings and the best methods of classifying and describing them. The first of these has to do with a small group of cases in which the onset of symptoms, the course and clinical signs of disease have all suggested strongly an acute or subacute inflammatory myelitis, but in which necropsy has not revealed any interstitial changes, cellular infiltration of the perivascular spaces or medullary tissues, but only toxic degenerative changes in the more



highly specialised ganglion-cells and nerve-fibres. This class of case has raised the question how far retrograde changes of the parenchymatous elements of the spinal cord can be properly regarded, in the absence of interstitial or vascular changes, as evidence of a myelitis. Schmaus states that the two characteristics of this type of case are: (1) oedema of the tissues, and (2) degenerative changes in the nervous elements. Whilst both are often found in association with the interstitial changes in the more common inflammatory myelitis, it is their occurrence alone which has provoked no little controversy in regard to the inclusion of such cases under the head of myelitis. Although v. Kahlden considered that inflammatory oedema of the tissues is sufficient in itself to justify the use of the term myelitis, Mager demands, as a criterion, infiltration of the vascular adventitia and perivascular lymphatics with small round cells. Any attempt to discuss the merits of such diametrically opposed views would be out of place here, and a solution of the question must be left for further investigation.

Finally, some reference must be made to "compression myelitis," a name brought into use for the purpose of describing the morbid changes in the spinal marrow which result from the pressure exerted by tumours, granulation-tissue, thickened meninges, or displaced bone. In the absence of infection by bacteria, it seems more correct to regard these changes as directly due to the evascularisation and ischaemia dependent on slow vascular occlusion, but the use of some such term as "compression ischaemia" is not likely to be generally adopted.

Such are the difficulties which underlie the use of the term myelitis, difficulties which are the natural outcome of increased and advancing clinical knowledge, of improved histological technique, and of the birth and growth of bacteriology. In the still imperfect state of our knowledge it appears desirable to retain the term myelitis for general use, and to classify the various forms in the following manner—(1) infective myelitis; (2) toxic myelitis; (3) syphilitic myelitis; (4) chronic myelitis. This method has the advantage of keeping in different classes conditions which are not only etiologically and anatomically, but, to a slight extent, clinically distinct from one another. Any attempt to use the site or extent of the lesion of the spinal cord as a basis for classification can only lead to confusion with regard to etiology and morbid anatomy.

**I. INFECTIVE MYELITIS.—Etiology and Pathogenesis.**—The causes of infective myelitis are not materially different from those of inflammation in other parts of the body, although for reasons which are not altogether clear, the spinal cord is only seldom affected in this way. Infective myelitis, then, is a *rare* disease, possibly more rare now than in the past. Looking at the medical records of thirty or forty years ago, the use of the term "urinary paraplegia" makes comparison difficult, but, making due allowance for the fact that in many instances bladder troubles were secondary to spinal disease, it appears possible that

myelitis following cystitis or other forms of pelvic sepsis was more common than it is now. This would be readily accounted for by the improvement in modern methods of guarding against infection.

The disease has no definite relation to age or sex, although young adults are probably its more frequent victims. It displays no epidemic, seasonal, or climatic proclivities, nor has it any special association with any specific fever. On the other hand, the onset of myelitis has occasionally been related to the course of one or other of these diseases. Sir T. Barlow, amongst others, has recorded a fatal case following an attack of measles; Auché and Hobbs, and Marinesco and Oettinger have described its association with small-pox. Lépine, Schiff, and others have seen myelitis as a fatal complication in enteric fever, and Lépine inclines to the view that a specific typhoid myelitis should be recognised. The connexion between gonorrhoea and myelitis in some cases has been noted by von Leyden, Sir W. Gowers, and others. It is very properly pointed out by Blocq that recorded instances of the association of myelitis with an acute specific fever must be carefully criticised before being accepted, at any rate those belonging to the period before the general recognition of peripheral neuritis as a cause of pronounced paraplegia.

There is another group of cases in which, without any special antecedent, the wide dissemination of the spinal lesion suggests its bacterial origin. Babes and Varnali record cases of paraplegia which they regard as shewing the infective nature of a myelitis. In one case the micro-organism of malignant oedema was found in other organs; in another a short streptococcus was obtained from the vessels, and some vessels of the anterior cornu were filled with streptococcic thrombi. These authors, as well as others, regard the existence of early changes in the small blood-vessels as evidence that the source of the disease was in the bloodstream, and must therefore be conveyed in the form of some virus thereby. Rosenthal and Thiroloix, in a case of streptococcic vegetative endocarditis, in which an acute paraplegia appeared in the last three days, found that the spinal cord was extensively softened in the dorsal region, and a culture of streptococcus was obtained from the lesion. In another case the same authors obtained the *Streptococcus pyogenes* from a focus in the mid-dorsal region of the spinal cord, and this organism, when inoculated into a rabbit's ear, produced a characteristic erysipelas.

In considering the causes of myelitis it may be presumed that the disease can arise in one of several ways:—1. As an extension from neighbouring inflammatory processes, particularly when the latter involve the meninges or vertebral column. A tuberculous form of myelitis occurs in connexion with spinal caries, and less frequently with tuberculous meningitis. Some degree of myelitis is often present too in cases of meningitis due to pneumococci, staphylococci, streptococci, *Diplococcus intracellularis*, and other organisms; but in these conditions the symptoms of myelitis are largely overshadowed by those due to the meningeal affection. On the other hand, infective myelitis is practically always

accompanied by some degree of meningitis caused by the same agent. It must then be regarded as an essential part of the disease.

2. As the result of an infection of the spinal tissues through the blood-stream. This may take place either as an incident in a general pyaemia, or as a purely local phenomenon, in which case trauma or chill may have some influence in determining its site.

3. As the result of an infection through the lymphatics. The possibility of this source of infection is based more on the analogy of experimental pathology than on verified cases of human myelitis. The investigations of Homén and others on animals prove that infection of the spinal cord may take place along the course of the lymphatics accompanying the spinal nerves, giving rise to foci of intra-medullary inflammation similar in all respects to those seen in the human cord. The paucity of evidence from clinical cases on this point would be remarkable were it not for the difficulty attending their elucidation, but Marinesco (17) has succeeded in tracing an infection of the spinal marrow by way of the neural lymphatics in a patient suffering from crural gangrene. The further investigation of such sources of myelitis might throw light on the pathology of spinal disease following cystitis and other infective conditions of the pelvic, abdominal, or thoracic organs.

Modern pathological knowledge does not allow of primary importance being attached to the influence of cold, injury, strain, or muscular effort in producing the disease, although it is possible that these may be of some predisposing value in certain cases. On the other hand, the incidence of myelitis upon pregnancy or the puerperium has been of sufficient frequency to attract the attention of writers upon the subject. In many such cases the description has not contained enough evidence to enable the reader to judge whether they should be included in the inflammatory or the syphilitic groups. Rhein describes one of the former type in the fifth month of pregnancy, and one of us has seen a similar attack in an early puerperal state. There is also a special type of myelitis which occurs in connexion with childbearing, and which will be referred to among the toxic varieties of the disease (p. 658).

Little is known of the *bacteriology* of myelitis, except that a considerable number of different organisms have been found in the spinal tissues. Increase of our knowledge is seriously checked by the fact that the life of most bacteria within the spinal cord appears to be very short. Marinesco has shewn by experiment that an infective myelitis can be produced by several of the ordinary pyogenetic organisms, and the latter have been demonstrated in human cases. Less easily identified cocci have also been found, as, for instance, in the case reported by Drs. T. Buzzard and Risien Russell. In their patient, and in another referred to by Dr. Risien Russell, the causal agent was a diplococcus bearing some points of resemblance to, but not identical with, the meningococcus. It is not very often that death takes place so early in the course of the disease that the bacteria within the cord can be successfully cultivated, and their characteristics determined. On the other hand, it is not unlikely that the more general



use of lumbar puncture as a method of clinical and bacteriological investigation in cases of acute spinal disease will materially increase our knowledge of the infective agents responsible for this form of myelitis.

**Morbid Anatomy.**—*Macroscopical changes* in the spinal cord in cases of infective myelitis are not easily overlooked, and are essentially the same in character whether the extent of the lesion suggests the use of qualifying terms, such as transverse, diffuse, or disseminated, for its more graphic description. A transverse myelitis is one in which the upper limits of disease are fairly well defined, and in which there is evidence that the whole transverse area of the cord is more or less affected at that level; the longitudinal extent of the disease may be anything from one to half a dozen segments or even more. The term “disseminated,” on the other hand, indicates the presence of two or more foci of disease separated by comparatively healthy intervening tissue. In each case the etiological and histological characters may be precisely the same.

The naked-eye appearances vary with the length of time which has elapsed since the onset of the disease. In the earlier cases the affected parts are much softened, sometimes actually diffuent, swollen, and oedematous, and generally hyperaemic. Haemorrhages may give a dark-red or brown colour to the cut surface after incision, and all definition between white and grey matter is frequently lost. The meninges overlying the affected areas carry congested blood-vessels, and not infrequently are the seat of a serous or even purulent exudation. In cases which have survived for a longer period the affected portions of the cord are still soft, but generally narrowed and shrunken rather than swollen, the meningeal covering being slack or wrinkled rather than taut or distended. There is less hyperaemia both in the meningeal sac and in the substance of the cord, old haemorrhagic foci being now represented by brown or yellowish patches. If the disease has been very patchy in distribution, scattered scars or deformities or small cysts may mark the sites of its incidence. By this time it will be possible to detect in the white columns the secondary degeneration of ascending and descending tracts at some distance from the morbid process.

*Microscopically* the characteristic features of acute spinal inflammation belong partly to the vascular elements, partly to the neuroglia, and partly to the true nervous structures. The relative importance of these features varies in individual instances, but in cases of infective or infiltrative myelitis, the condition which is now under consideration, the part played by the mesoblastic constituents of the cord is never insignificant.

**Vascular Changes.**—Looking at a section stained by logwood and eosin under a low power the most striking appearances are produced by the dilatation and engorgement of the blood-vessels, and by the excess of nucleated cells in their adventitial sheaths and perivascular spaces. More detailed examination of the cells crowding these spaces shews that the majority are almost identical with the lymphocytes of the blood in appearance, although it is more than probable that they are derived from the structures of the sheath rather than from the contents of the



blood-vessels. Plasma-cells, mast-cells, and polymorphonuclear leucocytes may also be present, but the proportion of the latter to the total number of cells varies very considerably, and must depend upon factors which are still far from being understood. If the lesion has been of some days' duration large globular cells, filled with the granules and fatty products of disintegration (the granular corpuseles of older writers), may also be seen in the perivascular lymph-spaces and their vicinity. Within the lumen of the vessels the normal relative proportion of red and white corpuseles may be maintained or, in places where blood stasis has occurred, leucocytes may be found clumped together in masses.

**Neuroglial Changes.**—The general substance of the cord has usually undergone considerable alteration. Some evidence of oedema is generally provided by the presence of spaces in the tissues, which may contain an amorphous granular material deposited from the albuminous fluid. The neuroglial cells themselves display marked signs of activity; they swell and proliferate; many may be seen with large rounded bodies containing two or more vesicular nuclei and perhaps some vacuoles. Among them may be found migratory cells, from which they are not always to be easily distinguished. Occasional zones filled with polymorphonuclear leucocytes may be observed in the tissues, but these are generally seen in the immediate neighbourhood of a large vessel. Haemorrhages in the tissues, masses of granular debris, and small areas of necrosis may also be detected.

**Neuronic Changes.**—The nerve-cells undergo modifications which may be partly influenced by the oedema or by the vascular changes, but which probably depend still more upon the toxic products of the invading micro-organisms. They become swollen, rounded, and homogeneous; their chromatin granules disappear, and their nuclei tend to approach nearer and nearer to the surface. The axis-cylinder processes are swollen and often broken. With the extrusion of the nucleus the cell-body quickly shrinks and breaks up, traces of its existence being very difficult to detect. In the white matter the earliest obvious changes are those which affect the myelin sheaths of the nerve-fibres. The latter become irregularly swollen and lose their power of staining by the Weigert-Pal method, but the Marchi method reveals the presence of fat. At the same time the axis-cylinders become thicker in diameter and more irregular in longitudinal outline. The loss of their myelin sheaths leaves them naked and unsupported, and in prepared sections a rarefied, vacuolated appearance is given to the tissues.

Evidence of a varying degree of meningitis in the form of cellular infiltration of the pia-arachnoid completes the picture of myelitis in the acute stages. Three weeks after the onset a Marchi preparation from the seat of disease reveals the fatty degeneration which has taken place and shews much of the fat being taken up by large granular cells of neuroglial origin. Sections from other levels of the cord stained by the same method display in a striking manner the ascending and descending degenerations in the white columns.

At a still later period these degenerations are visible only when the

Weigert-Pal method is used, and by this time the acute changes in the foci of disease have been replaced by those which are characteristic of attempted repair. The vessels have lost much of their cellular infiltration, but their walls are thickened and perhaps hyaline in appearance. Proliferation of neuroglia, with the formation of some fibrillated tissue, has taken the place of the nervous elements which have been destroyed, and possibly small cysts may be present, indicating areas of old necrosis. The number of vessels in the sclerotic zones suggests that there has been some new vascular formation in the course of healing. The secondary degenerations up and down the cord are still more evident, and if there has been extensive involvement of the anterior cornua, similar changes may be found in the anterior roots and the peripheral nerves, with atrophy of the muscle-fibres innervated from those regions.

**Symptomatology.**—In all cases of myelitis the clinical symptoms to a great extent depend upon the site and extent of the spinal lesion. The onset of infective myelitis is in most instances associated with some constitutional disturbances, pyrexia, loss of appetite, and vomiting being the most frequent. Burning pain in the back and paraesthesias, such as numbness or tingling, especially in the lower limbs, usually precede the onset of paralysis. The rapidity with which the latter reaches its height varies from a few hours to several days, and one symptom, such as retention of urine, may be noticed for a considerable length of time before others attract attention.

*The transverse* type of myelitis is not only the most common but is the best example upon which a description of the clinical phenomena may be founded. In every case a distinction must be drawn between the local symptoms, dependent upon the destruction or partial destruction of nerve-centres situated in the segments which are the seat of inflammation, and the remote effects produced by interference with the conducting paths passing through those affected segments. In this way the clinical picture varies with the segmental localisation of the disease, and it is imperative to consider separately the results of (1) a cervical, (2) a dorsal, and (3) a lumbo-sacral lesion.

1. **Cervical.**—A focal myelitis implicating the higher cervical segments is rare, and generally rapidly fatal owing to paralysis of the entire respiratory musculature including the diaphragm. There is of course partial or complete loss of voluntary power in the muscles of the neck and trunk as well as in those of all four limbs. Sensibility is lost or profoundly modified over the same areas, and control over the sphincters is deficient or absent.

More common are cases of myelitis affecting the cervical enlargement. If the eighth cervical segment corresponds to the uppermost level of disease, there is an atrophic flaccid paralysis of the intrinsic muscles of the hands and of the flexors of the wrists and fingers, while the extensors of the wrists and the muscles, subserving movements of the elbows and shoulders, remain intact. Involvement of the oculo-pupillary fibres at this level gives rise to small pupils, which do not dilate to shade, and to narrow

palpebral fissures. The condition of the trunk and lower limbs depends upon the severity of the lesion. If the latter is insufficient to cut off completely all impulses passing through it, a spastic paralysis of all muscles in the trunk and legs with the exception of the diaphragm is the result. Sensibility to all forms of stimuli is impaired or lost from the level of the area supplied by the eighth cervical segment downwards. There is retention of urine and constipation associated with incomplete control over the sphincter ani when aperients are administered. All abdominal reflexes are lost, the knee- and ankle-jerks are brisk, clonus may be obtained, and the plantar responses are of the extensor type. Paralytic distension of the hollow abdominal viscera may also be observed. The tendency to trophic changes and especially to the formation of bed-sores in the anaesthetic areas varies directly with the severity of the lesion. If, on the other hand, the morbid process is sufficient to prevent all impulses being conducted through the diseased segment or segments, the paralysis of the trunk and legs is not only complete but is flaccid in character, and is accompanied by absolute anaesthesia, loss of all tendon-jerks and plantar responses, and by total paralytic incontinence of urine and faeces.

The condition just described is naturally one of very great danger to life; any catarrhal trouble in the lungs is likely to prove serious not only because the diaphragm has to do most of the respiratory work, but also because abdominal distension may materially increase the embarrassment. Fatal complications may also readily arise from the supervention of bed-sores or from infection of the urinary system. In the spastic cases the patient's discomfort may be increased by the occurrence of painful flexor spasms of the lower extremities.

2. *Dorsal*.—In cases of dorsal myelitis the arms are not affected. Atrophic paralysis of the trunk muscles is not always easy to detect, and consequently the upper limit of the lesion is not easily defined by means of the motor symptoms. The upper border of the sensory disturbance, whether in the nature of hyp- or hyper-aesthesia, indicates better the highest level to which the disease extends in the spinal cord. When the lesion is situated about the ninth dorsal segment an attempt to sit up on the part of the patient may lead to drawing up of the umbilicus, indicating paralysis of the lower half of the recti abdominis; in such a case the upper superficial abdominal reflexes would be preserved and the lower ones lost. The paraplegia resembles that of the cervical cases; it is spastic with partial and flaccid with complete lesions. The state of the reflexes and of the sphincters corresponds to that described as occurring in the case of higher lesions.

If the inflammation is limited either to the right or left half of the transverse area of the cord, the clinical picture obtained is more or less that which is known as Brown-Séquard's paralysis. It is rare, however, for an inflammatory lesion to reproduce exactly the symptom-group characteristic of an experimental hemi-section of the cord.

3. *Lumbo-sacral*.—Cases of myelitis in this region of the cord



present symptoms which are limited to the lower extremities and to the vesical, rectal, and genital functions. In the purely lumbar cases there is rapid atrophic paralysis of certain groups of muscles associated with spastic paralysis of (segmentally speaking) lower groups; as in other forms of myelitis already described there is disturbance of sensibility both in the areas innervated from the affected segments and in areas supplied from the segments below. Retention of urine or precipitate micturition is accompanied by constipation with incontinence after aperients. In such a case the knee-jerks may be lost while ankle-clonus and the extensor type of plantar reflex may be readily obtained. If, on the other hand, only the lowest segments of the cord are diseased, the paralysis is altogether flaccid and atrophic in character; there is toneless relaxation of the sphincters, and loss of all reflex action and of sensibility within the areas innervated by the sacral segments.

In myelitis at any level of the cord it is the rule to find sexual activity in total abeyance, at any rate in the early stages; priapism is not uncommon with severe lesions above the lumbo-sacral region.

In discussing these various forms of transverse lesions we have used, for the sake of brevity, certain terms, such as "atrophic paralysis" and "spastic paralysis," which deserve rather more detailed explanation. "Atrophic paralysis" refers to that form of paralysis which is the result of a lesion of the lower motor neurons, and implies therefore not only loss of power but wasting and absence of excitability in the muscles innervated by those neurons. Such muscles are incapable of being made to contract either by direct mechanical stimulation or by tapping their tendons; they rapidly lose all response to the faradic current, and shew a slow contraction with the make and break of the galvanic current. Moreover, the anodal closure current is often more effective than the kathodal current in producing a contraction. Besides being atrophic these muscles are toneless and flaccid, and fibrillar tremors are occasionally noted on their surface. By "spastic paralysis" is meant that condition of the musculature in which partial or complete loss of voluntary power is associated with preservation of its nutrition and of its electrical excitability. Further characteristics of the affected muscles are that they are more rigid (hypertonic) than normal, and that they are readily excited to contract by mechanical stimulation applied to their surface or to their tendons. In these circumstances it is not surprising to find that they are liable to involuntary contractions, the so-called flexor spasms already alluded to as painful complications in certain cases of myelitis. Such is the hyper-excitability of the reflex mechanism under these conditions that minimal stimuli applied to the skin, even at some distance from the muscles, will evoke these spasms. Spastic paralysis is found in muscles innervated from segments of the cord which are in themselves healthy, but which lie below the level of a partial transverse lesion.

We have stated above that a flaccid paralysis is found in muscles innervated by segments of the cord below the level of a *complete* transverse lesion. The chief feature of this condition is the fact that although



flaccid and hypotonic these muscles do not waste or lose their electrical excitability until a much longer time has elapsed than is required for the same phenomena to supervene in instances of atrophic palsy. They may preserve their nutrition and excitability for weeks and even months after the onset of the disease which has physiologically cut them off from the higher nervous centres; but if the lesion is permanently complete there comes a time when they cease to respond to stimuli and begin to fail in nutrition. More frequently a lesion which is complete in the early stages, owing to the subsidence of inflammation and oedema, becomes less complete as time goes on, with the result that a flaccid paralysis becomes changed into one of the spastic type. It must be remembered that in this form of flaccid paralysis the tendon-jerks of the affected muscles are not obtainable, but that they too may return with the supervention of spasticity.

Although we are not yet fully acquainted with the laws which govern the disturbances of vesical and rectal functions, a few more details may be added to the facts already stated. In extensive lesions of the lower spinal segments there is always complete toneless relaxation of the sphincters, urine and faeces dribble away without the patient being aware of any desire to perform the natural functions, or being conscious that they have been carried out. In the case of lesions above the lumbo-sacral enlargement the condition of the bladder and rectum varies considerably with the degree of loss of expulsive power, of sensibility in regard to the contents of these organs, and, finally, of control over their reflex excitability. Thus, it is common to find in spastic paraplegia an initial retention of urine followed by reflex incontinence, and constipation followed by incontinence of faeces as soon as any attempt is made to empty the bowel by means of aperients. In other cases, the reflex excitability of the sphincter vesicae is more permanently lowered, and the constant use of a catheter is imperative for the purpose of giving relief.

The clinical pictures we have so far described represent the fully established disease in its earlier stages. A certain number of cases run a rapid course to a fatal termination, others last a few weeks, but succumb to some complication. In those which survive, recovery of function modifies in varying degree the initial condition. The victims of cervical or dorsal myelitis, although in rare instances regaining a more or less normal state of activity, usually present some degree of spastic paraplegia, which is either sufficiently severe to confine them to a bedridden existence, or may be so far alleviated as to allow of a partial resumption of the duties and pleasures of life. Bedridden patients have often to put up with the painful flexor spasms, the girdle sensation at the upper level of the paresis, and the loss of sphincter control which are characteristic of this later stage. Improvement in sensibility usually precedes and remains in advance of any improvement of voluntary power, and a case of this kind may live for many years and enjoy good general health if surrounding circumstances are favourable. Other patients in whom the disease has

not attained the same severity may gradually regain the power of walking, with perhaps the aid of a stick, and may recover sufficient control over their sphincters to be independent of catheterisation or even of a portable urinal.

In the lumbo-sacral type of myelitis the prospect of complete regeneration of the atrophied muscles is by no means bright, and the more serious interference with the bladder and rectum adds to the gravity of the outlook. Considerable degrees of recovery, resulting in a condition of partial disablement, not unlike that which follows lumbar poliomyelitis, may, however, be sometimes expected in those who survive the dangers attendant upon the early days of the disease.

From the clinical point of view it is very rarely that we can label as *disseminated* any case of myelitis. However multiple and discrete the foci of disease may appear to be at the necropsy, during life the picture is more often one of a transverse lesion corresponding to the level of the highest focus, or one of an acute ascending affection of the cord originating near its lower end. For the most part therefore disseminated myelitis is the anatomical description of what is clinically known as acute ascending myelitis, a name which for many reasons it is preferable to preserve. Very exceptionally it is possible to detect clinical evidence of more than one focus of inflammation in the cord, and perhaps rather more commonly a diffuse myelitis may be obviously associated with some intracranial lesion of a similar character. Thus, a patch of inflammation affecting the optic chiasma and giving rise to changes in the optic discs as well as to serious interference with vision may accompany the spinal disease, or others of the cranial nerves and their nuclei may suffer in the same way.

*Acute ascending myelitis* can be readily recognised during life. It is characterised by a progressive loss of voluntary power and sensibility beginning in the lower extremities and climbing up the body segment by segment until involvement of the respiratory musculature threatens or actually takes the patient's life. There is a marked similarity between most of the cases of this type of myelitis which have been recorded, and a short abstract of one which we have observed will emphasise all the essential features:—

A man aged forty-four had been well until August 1903. On the 3rd, 4th, and 5th of that month he noticed dull pain about his chest, and on the following day he experienced some weakness of the legs although he was able to continue his work. After leaving his bed on August 7, he was conscious that his legs were numb, found that he could not empty his bladder, but was able to walk a quarter of a mile. Inability to climb a ladder caused his return home, and the next morning he was unable to stand. On the 9th his legs were powerless, and he was insensitive to pins thrust into the skin anywhere below his ribs. Three days later he suffered from pains shooting down his arms, and this was followed within twenty-four hours by paresis of those limbs. On August 14 he was unable to sit up or turn in bed. The skin covering the trunk was pale and dry, a well-marked tache being obtainable on stroking. On the other hand,

his face and neck were flushed and moist. His lips and tongue were furred, foul, and dry. The patient was mentally clear but apathetic. The temperature was 101° F., the pulse 72, and the cardiac condition normal. Respiration was shallow, regular, chiefly diaphragmatic, and of a frequency of twenty-eight to a minute. There was not any spontaneous cough, and attempts to produce one were feebly carried out. The abdomen was distended. After much aperient medicine an uncontrolled flow of fluid faeces was obtained. A catheter was necessary to empty the bladder. The cranial nerves were normal in function, and the patient was able to move his head and shrug his shoulders. Both arms displayed complete flaccid palsy of movements at the wrist and finger joints, some diminished power of movement at the elbows and shoulders being still present. Respiration was carried on by the diaphragm and accessory muscles, the intercostal and abdominal muscles being totally paralysed. The legs were flaccid and completely powerless. No wasting, tremor, or fibrillation was present anywhere. He was conscious of numbness from the feet to the nipples and of a dull diffuse pain in his back. Painful and tactile stimuli were unperceived up to the level of the nipples, and were only partially recognised as high as the fifth cervical root-area. The sense of position was lost in all four extremities and no tenderness was elicited on squeezing the muscles. All deep and superficial reflexes were absent from the trunks and limbs, the jaw-jerk, however, being easily obtained. The patient died from increasing respiratory failure on August 16, within a fortnight of the first symptom of illness.

The necropsy shewed a diffuse inflammatory lesion, of varying degrees of intensity, extending from the lower dorsal and upper lumbar region to the medulla. An organism grown from the cord could not be identified owing to its extremely poor vitality on the ordinary culture media.

There are many similar cases on record, some of shorter and some of longer duration, some fatal and some resulting more favourably. The extension of the disease to the brain-stem may be indicated by the implication of cranial nerves before death, and the occurrence of optic neuritis has been recorded in non-fatal cases. The degree of meningitis accompanying the myelitis in these cases varies considerably; when it is intense the term meningo-myelitis is sometimes substituted for myelitis. Dr. Risien Russell found the same organism in two cases, one of which had and the other of which had not, signs of meningitis. Little is yet known about the bacteriology of these cases, but the more routine practice of lumbar puncture in their early stages may throw light upon this aspect of their etiology.

In these rapidly fatal cases of acute ascending myelitis the paralysis is flaccid from beginning to end, and no atrophy or electrical change may be observed before death occurs. In subacute cases which survive the early dangers, muscular wasting and alteration of electrical reactions may supervene in some parts, whilst others present a more spastic condition. This variability is due to the fact that the damage done by the disease is very patchy in its ultimate results, both white and grey matter being indiscriminately involved by the scattered foci.

II. TOXIC MYELITIS.—This form of myelitis is even more rare than  
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the acute infective form just described, which, as we have said, is by no means common. Moreover, it is very difficult to arrive at any trustworthy estimate of its relative frequency, inasmuch as there is a natural tendency to describe as "toxic" those cases of myelitis which make the most favourable recoveries, and in which, therefore, there is not any opportunity for verifying the diagnosis.

**Etiology.**—As yet there is very little trustworthy information concerning the origin of cases of toxic myelitis. On the one hand experimental pathology has shewn that a number of bacteria and bacterial toxins can, when introduced into the bodies of some of the lower animals, produce paralytic conditions which may reasonably be referred to the retrograde changes in the spinal cord found after death. There is reason to believe that the same organism may at one time, or in certain circumstances, incite an infiltrative, and at another time and under other conditions determine a toxic form of myelitis; but we are not fully acquainted with the laws which regulate such different results. It is equally certain that the effect of some organisms upon the spinal cord is in part to excite those interstitial changes which we regard as characteristic of inflammation, and in part to produce degenerative changes in the more specialised nervous elements. On the other hand must be mentioned the cases of toxic myelitis associated with pregnancy, which have been specially studied by v. Hösslin and by Rosenberger and Schmincke. According to these authors the myelitis is the result of an auto-intoxication which is often responsible at the same time for serious trouble in connexion with the cardiac and renal functions. In the next place there is good reason to believe that certain inorganic substances, especially lead, alcohol and some poisonous gases, may produce toxic changes in the spinal cord, but it is rare for the effects due to these agents to be confined to that part of the nervous system.

Landry's paralysis deserves separate consideration, because although toxic in character it has special clinical features which distinguish it from the ordinary diffuse or focal lesions of the spinal cord (*vide* p. 670).

**Morbid Anatomy.**—The toxic form of myelitis is only to be distinguished from the other forms by reason of its morbid anatomy, and it is unusual for the differential diagnosis to be made before the opportunity for actually estimating the histological changes is afforded, unless, as already suggested, the favourable course of a particular case of myelitis is regarded as sufficient justification for assuming its toxic character. In fatal cases the changes in the spinal cord, visible to the naked eye, are not, as a rule, striking; injection of superficial vessels, oedema, and some consequent loss in consistence of the tissues may be observed in recent cases, but even these may be absent after the acute stage has passed, and the evidence of secondary degeneration in the white columns may be scanty or completely lacking.

*Microscopically* the Marchi method brings out patchy areas of degeneration, chiefly in the longer white tracts, unaccompanied by any infiltration of the tissues or vascular adventitia by inflammatory cells.



Other methods of staining shew that the axis-cylinders as well as the myelin sheaths undergo changes in the direction of swelling and varicosity, sometimes passing on to complete destruction. The ganglion-cells of the grey matter present toxic retrograde changes of varying severity from slight chromatolysis to the enucleation which anticipates their final disappearance. Similarly the neuroglial cells display increase in bulk without that tendency to multiplication which is so characteristic of the infective form of myelitis.

In cases of long standing the only evidence of the preceding changes may be a "worm-eaten" appearance of scattered arcas in the white matter produced by the disappearance of groups of myelin sheaths, and diffuse secondary degeneration which follows no special systemic distribution.

**Symptoms.**—A complete description of the symptoms found in cases of toxic myelitis would be a mere repetition of those of infective myelitis (*vide* p. 652); it cannot yet be differentiated at the bedside. Reference to published cases suggests that an ascending form, subacute and slow in development, is not unusual, and that extension of the morbid process to the medulla oblongata is not unknown. The general character of the morbid changes found in fatal cases favours the view that the chances of complete recovery of function on the part of the nervous tissues are considerably greater in this form of myelitis than in any other form. With regard to the cases associated with pregnancy it is interesting to remember that v. Hösslin has recorded one in which the symptoms of myelitis recurred with each of several successive gravid states.

**III. SYPHILITIC MYELITIS. Etiology.**—There can be no doubt that syphilis is responsible for the great majority, probably eighty per cent, of cases of myelitis. Singer found that out of 19 cases of myelitis, admitted in the course of two years into the National Hospital for the Paralysed and Epileptic, 15 had a definite history of syphilis, and that in 12 the onset of paraplegia occurred within three years of the primary infection. Males are much more frequently affected than females, and the greatest susceptibility to this form of spinal disease prevails during the third, fourth, and fifth decades of life. The interval between the primary infection and the myelitis varies from a few months to many years, and it is probable that the shorter intervals are more common in younger subjects and in those persons who are imperfectly treated in the first instance. Syphilitic myelitis may also be the result of congenital lues, although this is by no means common.

In the majority of cases the incidence of the morbid process is on the dorsal, more particularly the middle third of the dorsal, region of the cord, probably on account of the paucity of large contributing root-vessels and the comparatively poor blood-supply in that area. This affords a point of contrast to the infective type of myelitis which favours the lumbar and cervical enlargements, where the blood-supply is rich, at least as frequently as the dorsal segments.

Although syphilitic infection must naturally be the chief etiological factor it is possible that fatigue, exposure, or alcoholism may be exciting causes, and that trauma may have some influence in determining the site of the lesion. This is a point of some medico-legal importance, but it is only fair to state that although this possibility may be admitted it is not supported by any scientific evidence of a convincing nature.

**Morbid Anatomy and Pathology.**—The considerable variation in the morbid changes found in cases which have presented almost identical clinical features is not so difficult to understand in the light of the versatile nature of syphilitic lesions in general. The virus produces its results in part by inciting changes in the walls of blood-vessels, with detrimental effects upon the local circulation; in part by the diffusion of toxic substances capable of exerting a profound influence on certain of the elements which it reaches; and in part by its power of provoking the formation of new tissue of an inflammatory or granulomatous nature. Any or all of these phenomena may be concerned in any particular case, but, as a general rule, one or other has a more or less preponderating influence. Moreover, it is important to remember that the relative implication of the meninges on the one hand and of the medullary substance on the other also varies very considerably.

In attempting to correlate the symptoms of a case of acute syphilitic myelitis with the post-mortem lesions it must always be remembered that morbid changes may have been silently at work for a considerable time before some sudden catastrophic, such as the occlusion of a blood-vessel, has provided an acute onset to the illness from the clinical point of view. A subacute or even chronic morbid process may thus appear to result in a very acute illness; in other instances the more chronic changes are manifested clinically by some of the premonitory symptoms which will be mentioned under Symptomatology. It is not surprising, therefore, to find after death evidence of syphilitic changes in the blood-vessels and meninges over a much wider area of the cord than the segment or segments which constitute the site of the lesion responsible for the clinical picture.

**Macroscopical.**—The site of the lesion is easily detected by a change in the consistence and perhaps in the calibre of the cord over one or more segments, the latter usually belonging, as has been stated, to the middle or lower third of the dorsal region. The medullary substance is softer than normal, and may even be reduced to a creamy fluid which readily escapes if the surrounding meninges are accidentally torn. In cases of some duration the calibre is much diminished and the pia-arachnoid is loose and wrinkled. Milky opacity of the soft meninges is observed at the site of the lesion, or may be general throughout the length of the cord. Not infrequently the dura mater is adherent to the subjacent membranes and can only be separated with difficulty. Atrophy of the anterior roots leaving the softened segments may be detected, and secondary degeneration of some of the white tracts may be seen above and below the lesion on cross section if the case has survived long enough.

**Microscopical.**—1. Blood-vessels.—There are three chief vascular

changes. In the first place moderate perivascular and adventitial cell-infiltration, with thickening of the intima, sufficient to produce diminution or complete occlusion of the vessel, may be general throughout the cord, or may be limited to the focus of disease. The round-celled infiltration may be slight and yet the walls of the vessels may be much thickened and hyaline. In the second place there may be excessive perivascular cellular infiltration with little or no endarteritis, in which case there is no evidence of actual obstructive thrombosis, although some blood-stasis is indicated by the excess of leucocytes in the vessels. Changes in the neighbouring tissues are in this case probably due to a toxic necrobiosis, or to an extension of the inflammatory cells from the precincts of the vessels into their midst. Thirdly and more rarely, there is a paralytic dilatation with slight perivascular infiltration and without obvious thickening of the vessel-walls. The general appearance produced by this change is one of hyperaemia, involving the white as well as the grey matter, and associated with retrograde changes in the nerve-fibres and ganglion-cells. Evidence of an inflammatory fluid exudation may be provided by the presence of an amorphous or perhaps colloid material within the tissue-spaces.

2. Neuroglia.—Within the territory supplied by vessels which are completely thrombosed the neuroglial cells and fibres share in the general necrosis, the former failing to stain with nuclear dyes, and the latter being no longer recognisable by special methods. Where the circulation is only partially interfered with, the neuroglial elements survive longer than the nerve cells and fibres, offering more resistance than the latter, and taking part in reparative processes. In these circumstances the neuroglial cells may be enlarged, rounded, and multinuclear; and, in later stages, they proliferate and send out interlacing processes in all directions. It is probable that they give origin to some of the large granular cells, so common in destructive spinal processes, which act as scavengers, and which, at first distributed in the tissues, are later collected in large numbers in the perivascular lymphatics. Along with the neuroglial changes must be mentioned the gummatous infiltration, spreading either from the vessels or from the pia and pial septa radiating into the cord. In some instances this forms the predominant feature in the morbid changes, and a true neoplastic gumma with central degeneration and caseation may occupy a considerable part of the transverse area of the section. In other cases, again, the appearance is that of a gummatous meningo-myelitis, either involving the cord in the form of a ring or penetrating its substance at a few points on its circumference.

3. Nervous Elements.—Demyelination of the nerve-fibres and retrograde changes in the ganglion-cells are the results of disturbed circulation or of the diffusion of toxic substances. In the course of the morbid change the myelin sheaths swell, disintegrate, and finally disappear, leaving the axis-cylinders in a naked, unsupported, but often swollen and varicose condition. The ganglion-cells undergo the usual changes in shape, in tigrolysis, and in nuclear displacement which are



common to other forms of myelitis. Such alterations are confined to the limits of the focal lesion and are not found in distant parts of the cord, although they may lead to secondary degenerations which can be traced through other parts of the central and peripheral nervous system.

4. The Meninges.—Round-celled infiltration of the pia-arachnoid is almost invariable, and is usually associated with various degrees of meningeal thickening. The arteries are often hypertrophied and the veins may display an obliterative phlebitis. The walls of the latter sometimes present a laminated appearance, layers of round cells being separated from each other by strands of fibrous tissue, with the result that their bulk is at least as great as that of the arteries.

Whilst the anatomical results of an acute or subacute syphilitic myelitis are often characteristic, the ultimate changes strongly resemble those in the later stages of other forms of myelitis. The processes of repair, of sclerosis, of formation of new vessels, and perhaps of cyst or cavity production, are essentially the same, and the examination of a focal lesion a year or more after the acute stage may not reveal anything to justify a definite statement as to its exact causation.

Although a focal transverse lesion limited to two or three segments is the most common change in syphilitic myelitis, multiple foci are by no means rare, and occasionally a few scattered patches of disease may invite the term "disseminated" for its description. Not infrequently a spinal lesion is associated with a cerebral lesion of the same nature, and we have seen several instances in which a spinal syphilitic lesion has complicated a parasymphilitic disease, generally tabes.

**Symptomatology.**—The onset of symptoms may surprise the patient while enjoying good health, or may supervene on a period during which he has been out of sorts, anaemic, and losing flesh. Without any obvious reason he finds that he cannot empty his bladder, or notices that one or both legs are heavy and weak, or numb and prickly. These phenomena may clear up within a few hours or a day or two, and are not unnaturally attributed to a chill. After a short interval he rapidly, sometimes suddenly, loses power in his legs, is unable to pass urine, and is conscious of a feeling of numbness from the waist downwards. A burning pain, localised to a point over the vertebral column, associated with a sense of constriction about the same level, may be experienced, but is by no means constant in the history of these cases. Constitutional disturbances are usually absent; the temperature is not raised and the appetite is often well maintained. In other cases one leg may be paralysed some hours or even days before the other, and occasionally the disablement is limited more or less completely to one lower limb, producing a modified form of Brown-Séquard's paralysis. In another variation of onset the patient, who has gone to bed in his usual health, wakes up in the morning paraplegic.

As the patient's condition is the same as that described in cases of transverse infective myelitis, it is unnecessary to refer to it again in the same detail. The paraplegia is flaccid or spastic in proportion to the severity of the lesion, and the amount of anaesthesia depends upon the same



factor. The bladder may need the use of the catheter, or may empty itself at intervals as an involuntary reflex act, or, later, owing to relaxation of the sphincter, allow of continuous dribbling increased by movements of the patient or by pressure on the abdomen. The anal sphincter is affected in a similar way, and incomplete priapism, exaggerated by attempts at using a catheter, may also be observed. The anaesthetic skin is dry and sometimes oedematous, and there may be a band of hyperaesthesia just above the level of the anaesthetic area. Of urgent importance is the liability to the appearance of bed-sores over the sacrum, on the ischial tuberosities, and on any point exposed to pressure or friction by bedclothes. Even in cases which are flaccid at first, spasticity is liable to supervene before many days have passed. The tendon-jerks become lively, ankle-clonus is obtained, and the extensor type of plantar response is easily elicited. Mere handling of the lower limbs or careless shifting of the bedclothes suffices to excite painful clonic spasms which draw the knees up and flex the thighs upon the trunk. Constipation and retention of urine with overflow incontinence are the characteristic sphincter troubles at this stage. In the more rare cervical and lumbosacral forms of the disease the symptoms resemble those in infective myelitis.

The examination of the cerebrospinal fluid, obtained by lumbar puncture, reveals an excess of lymphocytic cells. The fluid may be turbid and pale yellow in colour, and may yield a considerable precipitate on boiling. In some cases this fluid as well as the blood may give the Wassermann reaction for syphilis. Evidence of syphilitic lesions in other organs, or in other parts of the nervous system, may be found, and the presence of Argyll Robertson pupils should be particularly looked for.

The subsequent course of the disease depends upon a number of factors apart from the severity of the initial lesion. Under appropriate treatment and favourable conditions the spastic cases display a general tendency towards improvement, but in only a small percentage is recovery complete. Sensory disturbances usually clear up more quickly than the motor troubles, the greatest difficulty being generally found with the spasticity of the lower limbs, and the imperfect control over the sphincters. In favourable cases sexual power may be recovered even when it has been totally absent in the earlier stages. Fatal results supervene most often in cases in which the paralysis remains flaccid, and in which, for the same reason, sepsis from bed-sores or cystitis complicates the primary disease. In lesions of the cervical region respiratory paralysis adds to the dangers.

**DIAGNOSIS OF MYELITIS IN GENERAL.**—The subject of diagnosis in relation to myelitis may be conveniently divided into two parts:—(1) The diagnosis of myelitis from other forms of paralysis, and (2) the discrimination between the various forms of myelitis.

1. The conditions of paraplegia of acute or subacute onset most

likely to be confused with myelitis are those due to disseminated sclerosis, spinal compression, haematomyelia, haemorrhachis, hysteria, Landry's paralysis, and multiple neuritis.

An acute paraplegia, requiring only a few hours or a day or two for its evolution, is by no means rare in *disseminated sclerosis*, although it is very uncommon as the first manifestation of this disease. A careful history, therefore, is likely to disclose the previous occurrence of some other form of transient trouble referable to the central nervous system. The patient will recall some temporary diplopia, or amblyopia, or some difficulty with one limb, or some passing loss of control over the bladder in the past. Examination will probably fail to define a well-marked upper limit for the motor and sensory loss, and the presence of nystagmus, strabismus, pallor of the optic disc, or of some slight inco-ordination of the upper limbs will clear the way to an accurate diagnosis. In doubtful cases the cerebrospinal fluid must be examined; the absence of lymphocytosis will put myelitis out of court. Although disseminated sclerosis is never the result of syphilis, it occasionally occurs in a syphilitic subject; and this coincidence adds greatly to the difficulty of diagnosis. Even the improvement of symptoms under anti-syphilitic remedies must not be regarded as absolutely conclusive, on account of the remarkable spontaneous recovery which often takes place in the paraplegia of disseminated sclerosis.

The paralysis which results from *spinal compression* is in the large majority of instances gradual enough to exclude the possibility of its origin in myelitis, and where it is rapid there is usually some gross physical condition in the form of fracture-dislocation or caries of the spine to account for all the symptoms. It must be remembered, however, that paraplegia sometimes appears rapidly in cases of caries or malignant disease of the vertebrae without any spinal deformity, the cord being compressed by a mass of granulation-tissue, an abscess, or a nodule of growth. In these rare cases much care is required, and the help which can be obtained from the examination of the cerebrospinal fluid and from vertebral skiagraphy should be enlisted. The pain of myelitis, even in syphilitic cases, is rarely comparable to that experienced in compression of the spinal cord and its nerve-roots.

The rarity of *haematomyelia*, its almost invariable connexion with some definite injury or severe strain, and its extremely abrupt onset, are generally sufficient to allow of its differentiation from myelitis, although occasionally the diagnosis may be difficult. The intense radiating pain which is common in the former disease, and the rapid regression of symptoms during the early days after the onset, are also points which may prove of service in deciding the question. Still later the dissociated sensory disturbance so characteristic of haematomyelia will point in the same direction.

*Haemorrhachis* can be distinguished by the amount of pain experienced along the greater part of the spinal column, and by the preponderance of irritative over paralytic clinical phenomena. Occasionally,

however, a focal meningeal haemorrhage may simulate an attack of myelitis very closely, owing to the acute onset of paraplegia brought about by local compression of the cord. This is particularly misleading when the history of injury appears to be quite unimportant.

*Hysterical or functional paraplegia* may lead the unwary or inexperienced to a wrong diagnosis, although it is unhappily a more common error to regard the early stages of organic paralysis as hysterical in origin. If it be remembered that absence of the abdominal reflexes, absence of the knee-jerks, and the presence of the extensor type of plantar reflex always indicate organic disease, the mistake of diagnosing a case of myelitis as functional can rarely be made. A careful examination generally affords further evidence. The shifting upwards of the umbilicus during the attempt to sit up is certain proof of the organic nature of the lesion. If the legs are rigidly extended and remain fixed to the bed when the patient makes the movement just referred to, it is highly suggestive of a functional paraplegia. Incontinence of urine or faeces is not met with in hysterical cases, although there is occasionally some retention of urine. The power of discriminating between a true ankle-clonus and one which sometimes simulates it in functional conditions, is only acquired by constant experience, but the fact that in the case of pseudo-clonus the foot tends to follow the hand as pressure by the latter is gradually relaxed affords some help. Too much stress should never be laid upon the age or sex of the patient, the history of previous neurotic tendencies, or the presence of hysterical stigmata, many of which are common enough in cases of organic disease. A lumbar puncture, although it may be desirable for other reasons, should rarely be necessary to decide the question under discussion.

The only form of myelitis which is at all likely to be mistaken for *Landry's paralysis* is the acute ascending type, and no difficulty should be experienced in separating these two conditions if the constant presence of more or less profound sensory and sphincter disturbance in the myelitic patients is impressed upon the observer's mind.

*Multiple Neuritis*.—Not very many years ago the distinction between a paraplegia of spinal and one of neuritic origin was considered a prerogative of the expert; at the present day it is hardly necessary to recite the points of difference between the clinical manifestations of the two morbid processes. In the dorsal and cervical forms of myelitis the paraplegia is either spastic or flaccid. If it is spastic it cannot possibly be due to disease of the lower motor neurons; if it is flaccid the loss of motion and sensation below a certain well-defined level is far more profound and universal than is ever seen in multiple neuritis. Moreover, the sphincters are rarely affected to a severe extent in the latter disease. In cases of lumbosacral myelitis the resemblance to severe neuritis of the lower extremities may be superficially strong, and the differentiation will depend on the recognition of various points, such as the following:—In the myelitic cases the sensory loss is of the segmental type, bounded by lines which correspond to the limits of segmental areas, is more profound,



and involves all forms of pain and temperature to an equal extent; in neuritis the sensory disturbance is rarely so marked, has less defined limits, and is usually distributed peripherally and symmetrically over the stocking areas. In addition a considerable degree of deep muscle-hyperalgesia is often associated in the same part of the limb with cutaneous analgesia, a combination of symptoms which is not met with in the spinal cases. The sphincters in lumbo-sacral myelitis are completely relaxed; in multiple neuritis they are either unaffected or only partially uncontrolled. Finally, the cases of multiple neuritis, sufficiently acute in onset to suggest a myelitis, are the exception and not the rule.

2. A diagnosis of transverse myelitis having been arrived at, the question whether the case is of syphilitic or other origin has next to be decided. The history or absence of history of luetic infection must necessarily influence the answer to this question, and positive evidence of the disease will often help the medical man to a correct decision. In cases of doubt the mode of onset may be of some assistance. Premonitory symptoms are often observed over a considerable period of time before the definite onset of the myelitis in syphilitic cases, and the initial stage is generally free from constitutional disturbance. In the infective type, on the other hand, warnings are less common, and, when they do occur, precede by only a few hours the onset of paralysis. Moreover, some degree of general malaise, pyrexia, anorexia, and perhaps vomiting, is the rule rather than the exception in these patients. The site of the lesion is not of much diagnostic significance in this connexion, but, *ceteris paribus*, the dorsal region favours the syphilitic, and the cervical enlargement the infective, form of myelitis. The examination of the cerebrospinal fluid may, or may not, help to answer this question, but the presence of non-syphilitic organisms, or the discovery of the *Treponema pallidum*, would of course be decisive. A polymorphonuclear leucocytosis would suggest an infective case, but a lymphocytosis would not prove absolutely the syphilitic nature of the lesion. The Wassermann test should also be employed. If syphilis is suspected, without a clear history of the primary chancre, a careful search must be made for corroborative evidence in other parts, especially as regards the pupillary light-reaction. It must be remembered that a myelitis represents, not infrequently, one feature or phase of severe cerebrospinal syphilis, and that it may be associated with one or other of the parasymphilitic diseases.

When some infective process is suspected, every effort should be made to discover a focus in other organs from which the cord may have been secondarily invaded, and the presence of gonorrhoea or of septic conditions in the pelvis, abdomen, or thorax must be excluded. The association of this form of myelitis with some general disease such as enteric fever, measles, or small-pox must not be overlooked. As already mentioned the infective and toxic forms of myelitis cannot be differentiated clinically.



**PROGNOSIS.**—The outlook in cases of myelitis has already been indicated to a certain extent in describing the symptoms, but there are some points which may be of use in forming a prognosis in individual instances of the disease. The severity of the initial lesion is of importance both in regard to the prospect of recovery from the acute stage and in estimating the degree of return of function which may reasonably be expected in those who survive the immediate dangers. A complete loss of conducting power in the cord at the site of the lesion, even when it is only temporary, is a menace to life, and the higher the level of this lesion the greater is the fear of fatal complications. Interference with the respiratory mechanism may lead to a rapidly fatal termination in the cervical cases, especially in patients past middle age; and even when the dorsal region is the part affected, the tendency to severe bed-sores and to cystitis with renal infection constitutes a grave element in the struggle for life. Should the patient survive these dangers the prospect of good recovery of function is poor only, although in some of the toxic and syphilitic cases the result may be far more favourable than the early symptoms appear to warrant. Instances of lumbar myelitis are particularly hopeless with regard to regaining the power of locomotion, and the sphincter troubles not infrequently determine a fatal ending within a comparatively short period. The less complete cases of paraplegia may be confidently expected to shew marked improvement; but only after the effects of treatment, especially in the syphilitic patients, have been gauged, can any precise estimate of the result be arrived at. It must be admitted that cases of spastic paraplegia resulting from myelitis are often disappointing to their medical attendants. Improvement sets in and progresses up to a certain point, and then, when hopes of further success appear to be justified, a stationary condition supervenes and proves obstinate to all forms of further treatment. Dissatisfying as this must be, it can only be expected from our knowledge of the poor regenerative capabilities of the medullary tissues and of the sclerotic processes which inevitably follow upon severe inflammatory and vascular disturbances in the central nervous system.

**TREATMENT.**—*Infective and Toxic Cases.*—In the acute stage the patient must be absolutely at rest, preferably, and often imperatively, on a water-bed. Changes of posture may be necessary for the prevention of trophic sores, but cannot be seriously recommended for any influence they can exert upon the morbid process. The supposition that the volume of blood at the seat of the spinal lesion is lessened by placing the patient in the prone position, or that such a depletion, if it occurs, is beneficial, does not appear to be well founded. The effect of gravity in altering the hyperaemia must be insignificant, and, on the other hand, the determination of blood to the site of the lesion must be regarded as an essential factor in Nature's effort of resistance. Immediate attention should be paid to the bladder, and the urine should be drawn off if there is retention. Free action of the bowels should be secured at least every alternate day after an initial purge, and the greatest care must be taken

to keep the skin clean, especially in the perineum and at all points of pressure. If pyrexia and pain are present, a diaphoretic mixture containing salicylates or quinine, and a light fluid diet, are indicated. There is no reason to believe that the application of heat or cold to the spine can be of use, and disturbing the patient for the purpose of cupping is probably more harmful than beneficial. A lumbar puncture should be performed at the earliest opportunity, and a microscopical as well as bacteriological examination of the fluid carried out. Only on such lines can any hope of combating the disease be expected, and until this is a matter of routine practice little progress in treatment can be looked for.

As soon as acute symptoms have passed off, all paralysed parts should be rubbed and moved every day, and each joint prevented from becoming fixed. This measure and a tonic of iron and arsenic are the only general methods to be employed, although certain symptoms must be met by appropriate remedies. In the dorsal cases the spastic muscles do not need any treatment, but in the lumbo-sacral cases the atrophied muscles of the lower extremities should receive electrical treatment provided that this can produce contractions, the form of current being chosen according to the reactions. A careful watch must be kept upon the urine, and any sign of cystitis combated by means of urotropin by the mouth and by irrigation of the bladder with some antiseptic lotion. In the less severe cases the sphincter trouble may be favourably influenced by belladonna internally, and the same drug combined with extract of ergot may relieve the painful flexor spasms which so often cause suffering in this disease and which are sometimes very difficult to treat successfully. These spasms are particularly liable to be troublesome at night, and when sleep is much disturbed by them the use of such drugs as veronal, sulphonal, hydrobromide of hyosine, and even morphine on occasion is not only justifiable but urgent.

As the patient gains in strength, more energetic massage and passive movements may be carried out, and he should be encouraged to make every endeavour to perform movements on his own account. It is his duty to force impulses, as it were, through the block on the conducting lines or to find some other way round for the resumption of traffic. This side of the treatment is apt to be forgotten in the modern craze for massage and electricity. If the patient can be induced to attach less importance to the energy displayed by the rubber and to impart more energy into his own efforts at initiating voluntary movements, the medical attendant will have gained valuable co-operation in his task. When the limit of improvement by these means appears to have been reached, a change of air to some suitable health resort should be advised.

*Syphilitic Cases.*—The general treatment of these cases, as regards the prevention of bed-sores and cystitis, and the preservation of nutrition in the limbs, is similar to that already described. Antisyphilitic treatment can in most cases be commenced as soon as paralysis sets in, or better still, during the premonitory stage. Both mercury and iodide of potassium should be given, the method of their administration being of minor import-

ance. Beginning with 5 grains three times a day, the iodide should be increased rapidly until 20 or 30 grains are taken in each dose. The mercury may be given by the mouth in the form of perchloride or the red iodide, by inunction, or by hypodermic injection, but it is not advisable to apply the inunction or the injection to anaesthetic parts. This form of treatment should be pushed to the point of salivation and renewed after an interval of two or three weeks. Bearing in mind that the victim of syphilitic myelitis is prone to other manifestations of cerebral or spinal syphilis, and that there is no criterion to indicate when that liability is successfully eradicated, the medical adviser should insist on his patient undergoing a course of mercurial treatment two or three times a year for an indefinite period. Freedom from further syphilitic lesions may be secured in this way by the simple administration of grey powder for a few weeks at a time at the stated intervals. It must be admitted, on the other hand, that there are instances of syphilitic myelitis in which these remedies are of no avail, although they form the exceptions to the rule.

It is doubtful if any other drugs can take the place of mercury and the iodides in the treatment of the syphilitic lesions<sup>a</sup> of the cord, although atoxyl and other arsenical compounds deserve a trial, and may, at any rate, be used in the intervals between the courses of mercury and iodides.

IV. CHRONIC MYELITIS.—This term, which is becoming obsolete, can only be used to describe the chronic and stationary stage of cases of myelitis, of acute or subacute onset, when partial recovery has taken place. Instances of slowly progressive spinal disease which deserves the name myelitis are sometimes seen in connexion with syphilis (Erb's syphilitic paraplegia); these are described elsewhere (p. 726).

The term is not generally applied to the spinal sclerosis, such as tabes or Friedreich's disease, in which it is probable that the primary lesion is degenerative and the inflammatory element, if present, only secondary. Disseminated sclerosis, on the other hand, has some claims to be regarded as a chronic inflammatory disease of the spinal cord, and is sometimes held to be the only true instance of chronic myelitis.

We have already described the symptoms and morbid anatomy characteristic of the chronic stage of cases of myelitis, and it is unnecessary to repeat here what has been stated. The question of diagnosis has also been discussed, and emphasis has been laid upon the danger of regarding as examples of chronic myelitis those cases in which a spinal tumour is responsible for the symptoms of slowly progressive paraplegia.

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## LANDRY'S PARALYSIS

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**History and Introduction.**—In 1859 Landry described the following case of acute generalised paralysis which ran a rapid and fatal course in rather less than two weeks:—

A labouring man, aged forty-three, who had been in very indifferent health for a year before his death, complained, for a few weeks preceeding the onset of any definite paralysis, of tingling in his fingers and toes, and of general weakness which, however, did not prevent his walking a considerable distance to the hospital where he came under observation on June 1, 1859. On June 13 his legs began to fail, and the tingling sensations spread towards the proximal parts of his upper and lower extremities. In a few days all four limbs were more or less completely paralysed, and after a short interval the muscles of the



trunk, and especially the diaphragm, shared in the general loss of power. There was no pain, and his mind remained clear. The temperature was not raised, and the actions of the bladder and bowel were unimpaired; but the reflexes were lost, and there was some blunting of sensibility in the peripheral parts of the limbs. The paralysed muscles responded to the faradic current, and did not shew any tendency to contracture. With increasing respiratory difficulty some weakness of the masticatory muscles and of the tongue appeared, although all the movements of the face and eyeballs were normally performed. A sense of constriction round the thorax and numbness in the limbs were described in addition to the tingling already referred to. The patient died quite suddenly on June 25 while he was being propped up in order to take food. With the exception of pleuritic adhesions no gross changes were detected at the necropsy. A careful microscopical examination of the spinal cord failed to reveal any morbid process; the peripheral nerves were not investigated.

During the fifty years since this classical case was published nearly all the cases of acute ascending paralysis bearing any resemblance to its clinical features, and irrespective of their morbid changes, have been included in the category of Landry's paralysis. At the present time it is generally recognised that the irresponsible use of this name has led to such a state of confusion in the literature of the acute forms of paralysis that any effort to extricate the cases which have from the cases which have not deserved the term is almost fruitless. This unfortunate confusion has originated for the most part in three ways: (i.) Many cases of acute poliomyelitis in adults have been mistaken for Landry's paralysis during life, and the diagnosis has not been revised when microscopical examination of the spinal cord has revealed the inflammatory changes characteristic of the former disease. (ii.) The undoubted occurrence of instances of toxic polyneuritis has led some observers to believe that Landry's original case was of this nature. The absence of any examination of the peripheral nerves renders the denial or confirmation of such a possibility equally unjustifiable. (iii.) The disease known as acute ascending myelitis presents features which have been responsible for the diagnosis of Landry's paralysis in certain instances.

I am anxious to avoid what could only be an unsuccessful attempt to reconcile the various views which have been and are held upon this question, or to classify the different morbid processes which have at one time or another been styled Landry's paralysis. It will certainly never be known what was the actual disease from which the cases recorded by Landry suffered; and it is sufficient for our purpose that he called attention to a class of case in which the symptoms were those of a rapidly spreading motor paralysis, without atrophy or electrical changes in the muscles, with slight sensory phenomena and no sphincter disturbances, and in which he was unable, by the methods at his disposal, to detect anatomical changes. Does this class of case still exist? The answer to this question is in the affirmative if allowance is made for improved histological technique, and if it is not forgotten that Landry was certainly in a position to detect the changes of acute poliomyelitis or

any other acute inflammatory process in the spinal cord. It is clear, however, that acute ascending paralysis and Landry's paralysis cannot be regarded as synonymous terms; the latter is only one variety of the former.

It will be the object of this article to describe a morbid condition bearing a strong clinical resemblance to that of Landry's cases, in which the anatomical changes in the spinal cord would certainly have escaped notice with the methods of fifty years ago, and which does not appear to call for inclusion within the group of the neuritides. There is nothing to be gained from imitating the course adopted by some writers, who describe a central and a peripheral form of Landry's paralysis; the peripheral form can only be regarded as a polyneuritis.

**Etiology.**—There are but few points of etiological importance in relation to Landry's paralysis if we exclude those cases which should properly be classed under the term myelitis. A history of some infective disorder, such as gonorrhoea, influenza, or enteric fever, is sometimes met with, but not with sufficient constancy to merit attention. In the majority of instances the disease attacks healthy adults, and the period of life between twenty and forty years of age appears to be that in which persons are most susceptible. Men are more often affected than women, but it is difficult to say whether the preponderance is great or insignificant. Exposure to extremes of heat or cold may be a predisposing factor; in one case the patient was a printer who had recently worked in close proximity to a hot stove, and stood on a hot floor (4). Seasonal or climatic influences are not known to play any part in the incidence of the disease, nor is there any evidence that it occurs in epidemics. During epidemics of acute poliomyelitis, however, the earlier severe cases have often been regarded as examples of Landry's paralysis until examination of the tissues has revealed the true condition.

The bacteriology of Landry's paralysis is in an immature condition, and it is not possible to say whether the disease is specific or whether it may occur as a result of various forms of intoxication, bacterial or otherwise. The large majority of cases in which spinal lesions have been absent or insignificant have given a negative result on bacteriological investigation. On the other hand, a few have provided data of some significance. In a case of acute ascending paralysis Roger and Josué found toxic changes in the cells of the lumbar enlargement; and although suitably stained sections did not demonstrate the presence of any organism, cultures from the heart's blood shewed a diplococcus resembling the pneumococcus. Injections of the cocci into a mouse did not prove fatal, but a rabbit submitted to the same experiment died after twenty-one days with paraplegia, and the organism was recovered from its blood. In a case in the National Hospital under Sir W. Gowers I found (i.) a micrococcus in pure culture from the blood of the patient after death; (ii.) an organism indistinguishable from (i.) in large numbers in the loose vascular tissue forming the external layer of the spinal theca; (iii.) that subdural injection of the cultivated cocci into a rabbit produced after some days a rapidly

spreading palsy ; (iv.) that the same organism was present in the theca of the rabbit, and could be isolated in pure culture from its blood ; (v.) in neither the patient nor the rabbit was the organism demonstrated in the spinal cord or the pia-arachnoid, and in neither case were there inflammatory reactions in these tissues. Drs. Maenamara and Bernstein isolated from the blood and cerebrospinal fluid of a non-fatal case a coccus somewhat resembling that just described, but they failed to obtain any positive results from experimental inoculations.

It may be almost certainly assumed that if the disease is due to some bacterium the latter does not infect the cord itself, but exerts its influence either through the blood or the lymphatic system. In all cases, therefore, the blood and cerebrospinal fluid should be examined during life, and the extra-theal tissues if death occurs.

**Morbid Anatomy.**—Naked-eye examination of the central and peripheral nervous tissues generally shews nothing except some hyperaemia of the spinal cord. In the absence of post-mortem changes the cord is firm and natural in consistence, although the vascularity of the grey matter may be obviously increased. Small haemorrhages, such as are not uncommon in any case of death from respiratory failure, may be noticed in the nervous as well as other tissues. The cerebrospinal fluid is abundant and clear, and the soft meninges do not present any signs of inflammatory or suppurative exudation.

Examined by the ordinary methods of staining, the cord appears normal except for a few capillary haemorrhages, but if the Nissl and Marchi methods are employed a careful inspection of a large number of sections usually reveals the following changes : (1) Cells—A smaller or larger number of cells, especially those of the anterior horns and of Clarke's column, present either early pericentral chromatolysis, or more or less complete loss of chromatin granules and eccentrication of nuclei. The most intense changes in the cells occur in those parts which, judging from the clinical symptoms, were earliest affected ; in the majority of cases the legs are the first limbs to fail, and the most marked cellular changes are detected in the lumbo-sacral enlargement. (2) Myelin—The myelin sheaths of the nerve-tracts in the spinal cord, and to a less extent those of the peripheral nerves, often present a form of diffuse fatty change when examined by the Marchi method. In longitudinal sections small droplets of fat are seen lying singly, or two or three together, along or between the nerve-fibres, and do not fill the transverse area of the myelin sheaths. This appearance may be found in toxic states unassociated with paralysis, and does not therefore indicate necessarily any functional alteration in the nerve-fibres. (3) Neuroglia and Vessels—There is no evidence of neuroglial proliferation, although some of the cells may appear larger or more globular than normal. The vessels are engorged, but are free from changes in their walls or perivascular sheaths. Very rarely a slight excess of small round cells may be seen in the immediate neighbourhood of one or two vessels. The above are the only morbid changes found in most cases at the time of death. Occasionally,



when the fatal termination has been postponed, the Marchi method will reveal the presence of some fibres undergoing true Wallerian degeneration in the spinal cord and peripheral nerves, probably secondary to the cell changes. It should be noted that these morbid appearances in the nervous tissues could not possibly be detected by the methods available when Landry worked at the subject.

Early fatty changes in skeletal muscles are often detected, but definite atrophy is not present. Apart from the neuro-muscular tissues, the most constant changes have been an enlarged spleen, enlarged mesenteric glands, and some evidence of pulmonary or pleural complications, generally of a secondary character.

**Symptomatology.**—The disease is often ushered in by a distinct prodromal stage lasting some hours, days, or even weeks, during which there may be various subjective sensations. Pain in the back is occasionally, although not commonly, present, but pricking, tingling, numbness, or pins and needles are usually described and referred to the peripheral parts of the limbs. A general sense of languor or fatigue and a feeling of heaviness in the legs and arms may also precede any definite loss of power.

The onset of paralysis takes place somewhat rapidly and smoothly, or by definite stages. In the latter case there may appear to be stationary periods followed by rapid involvement of fresh areas. Usually the legs are affected first, but occasionally the arms, and rarely the cranial nerves, present the earliest signs of the disease. The paralysis spreads from one part to another, following roughly the lines of spinal innervation. The lower intercostal muscles, for instance, fail before the diaphragm is affected, if the disease is following an ascending course, and the peripheral parts of the arms suffer before the muscles of the shoulder-girdle. When a whole limb has become paretic, however, the proximal muscles are just as powerless, or sometimes even more powerless, than those moving the hands or feet. I have on more than one occasion seen a patient perfectly helpless as regards any gross movement of the trunk or legs, yet able to flex and extend his toes slowly. In this respect the condition affords a most striking contrast to that seen in multiple neuritis, in which as a general rule the peripheral muscles are more paralysed than the proximal.

Throughout the whole course the paralysis is of the flaccid type, the muscles lacking their normal tone and presenting no opposition to passive movements of the joints. No atrophy can be detected in any muscle until at least two or three weeks after the onset, and even then the wasting is very evenly distributed and very slightly marked. Their excitability to the faradic current is also usually well preserved, although a stronger current may be required if the patient survives three weeks of paralysis.

With the gradual upward extension of the process the movements of the head, and later those of the tongue, larynx, pharynx, and palate, may be more or less seriously interfered with. It is unusual, however, for a



patient to live a sufficiently long time, after the respiratory musculature has become embarrassed, to develop cranial nerve symptoms of marked degree. Inactivity of the accessory muscles of respiration, difficulty in swallowing and in articulation, are the principal complications brought about by the spread of the disease to the bulbar centres, and, of course, add greatly to the gravity of the condition. The paralysis of the neck and trunk, as well as of all four limbs, renders the patient extraordinarily helpless, the helplessness being often emphasised by comparison with his general appearance of good health and his perfectly clear mental condition.

In contrast to the severity of the motor symptoms everything else appears almost insignificant. Constitutional disturbance may be slight or even absent, and the temperature rarely exceeds  $100^{\circ}$  or  $101^{\circ}$  F., unless it rises rapidly within a few hours of death. The intellect and memory remain unimpaired so long as respiration is effectively carried on, and, in spite of dyspnoea, the patient is usually cheerful and sanguine concerning his condition. The paraesthesias associated with or preceding the onset may continue for some time, and, in addition, there may be cramp-like pains in the immobile limbs, which are generally relieved by change of posture.

As a rule cutaneous sensibility is normal; occasionally the appreciation of light touch may be blunted in the peripheral areas of the extremities. Deep sensibility is often slightly increased, although there is not that degree of muscular tenderness which is so characteristic of peripheral neuritis. The sense of passive movement and position remains unaffected. All the deep and superficial reflexes are absent in the paralysed parts, and usually disappear with the onset of any decided paresis. The plantar response remains flexor in type so long as it can be elicited at all.

The rectal and vesical sphincters are unaffected, although, from paralysis of the abdominal muscles, there may be some difficulty in emptying the rectum and bladder. Incontinence does not occur, except as the result of a distended bladder, and the patient is conscious of the natural calls to defecation and micturition.

With ordinary care bed-sores can be avoided, as there is no special tendency to their formation nor any deficiency in healing power. Vasomotor disturbances are slight, if present at all; the skin over the paralysed parts is moderately moist, at any rate in the early days of the disease. A tache may sometimes be elicited.

It is often remarkable how little the patient's cardiac action is affected, the pulse maintaining fair strength and regular rhythm long after respiration has become difficult. In fatal cases the respiratory muscles give out a considerable time before the circulation fails, and the employment of artificial respiration may often prolong life for many hours if persevered with. In Landry's original case, on the other hand, sudden syncope appears to have been the actual cause of death. If life is prolonged, the most serious complications are pulmonary or bronchial

catarrhs, with which the patient, owing to his weakened respiratory muscles, is hardly fit to cope.

When neither the disease itself nor any complication proves fatal, the patient enters upon the stage of recovery, which often presents some features of interest. The muscles may shew a moderate degree of general wasting within three or four weeks of the onset of the disease, but the atrophy is diffuse, and not limited to particular muscular groups. The response to faradism may be diminished, but is very rarely lost, and the galvanic current produces a normal or slightly sluggish contraction. Recovery of power and nutrition takes place slowly and equally over the whole of the musculature, and it is rare for any particular set of muscles to hang behind the others in their rate of progress. Occasionally those of the limbs do not respond to treatment as quickly as those of the trunk. Contractures and deformities are rare, except as the result of neglect. Remissions and recurrences are not known to occur; and when the process of recovery has begun, the patient may look forward as a rule to complete return of normal health and activity.

**Prognosis.**—The confusion which has existed with regard to the classification and recognition of cases of Landry's paralysis renders it impossible to give reliable statistics as to the mortality of the disease. In my opinion Landry's paralysis is a very fatal disease, and in this respect contrasts unfavourably with acute toxic polyneuritis and also with acute poliomyelitis, although the severe cases of the latter disease, which most resemble Landry's paralysis during life, often terminate in death.

Some instances of true Landry's paralysis, however, undoubtedly end favourably, and there is then no reason to expect anything but an exceedingly good or even perfect recovery of function. The gravity of any particular case depends almost entirely on the condition of the respiratory musculature. So long as the diaphragm and the accessory respiratory muscles are intact, or at any rate capable of considerable work, there is, in the absence of complications, no cause for anxiety. When the diaphragm and intercostals are very feeble, and the respiration is carried on largely by the sterno-mastoids and other neck muscles, the appearance of cyanosis, the look of distress, and the fogging of the patient's intellect are danger-signals of the gravest import. The most favourable cases are those in which, although the muscular feebleness is very general, the loss of power is nowhere complete. Pulmonary and bronchial troubles, even after the acute stage has passed, must always be regarded as serious, but few cases survive the primary disease to die from complications.

The **diagnosis** of Landry's paralysis is important, not so much from the point of view of treatment in the present imperfect state of our knowledge, as for the purpose of giving an accurate prognosis while the disease is still in its acute stage.

When a patient is suddenly seized with an acute form of paralysis involving a large part of his musculature two questions may well be

asked by his friends: "Is he going to live?" "If he lives, will he be permanently disabled?" The medical attendant will naturally ask himself, "Is this a case of acute ascending myelitis, of acute poliomyelitis, of acute toxic polyneuritis, or of Landry's paralysis?" Upon the answer to these questions the prognosis must largely depend. For instance, the diagnosis of acute toxic polyneuritis renders the prognosis bright as regards both life and fair recovery of power; whereas in acute poliomyelitis the prognosis is hopeful as regards life, but very grave as regards return of activity.

There should be no difficulty in distinguishing cases of *acute ascending myelitis* from those of Landry's paralysis on account of the severe sensory loss and sphincter disturbances of the former condition, although the spread of motor palsy is often similar in the two diseases.

*Acute and widespread poliomyelitis* has often been diagnosed as Landry's paralysis, but attention to the following general principles will assist towards a proper diagnosis: (1) The constitutional symptoms in the severe cases of acute poliomyelitis are more marked than those in Landry's paralysis, the range of temperature is higher, often reaching  $102^{\circ}$  to  $104^{\circ}$  F., the malaise and anorexia more profound, vomiting and disturbance of the alimentary canal more frequent. In children convulsions are often associated with the former ailment. The older the patient the less likely is acute poliomyelitis to be present. (2) Sensory Phenomena—In Landry's paralysis there may be, and often is, complaint of pain in the back, of sensations of numbness and tingling in the extremities before and during the onset of paralysis. The only sensation complained of in the paralysed limbs is that of vague discomfort or cramps, arising, partly at any rate, from their immobility; they may be handled without giving rise to anything more than slight tenderness on deep muscular pressure. In acute poliomyelitis the pains complained of are more urgent, and affect not only the back, head, and neck, but frequently the limbs as well. Paraesthesias may be present, but the more prominent feature is the pain, sometimes very severe, elicited by passive movements of the affected extremities. In both diseases cutaneous sensibility is usually unimpaired. (3) Motor Phenomena—In both diseases paralysis is flaccid and may be general. The escape of a single muscle or of a group of muscles in a region where all the others are affected, or a marked asymmetry in the condition of corresponding muscles on the two sides of the body, are points suggestive of acute poliomyelitis rather than of Landry's paralysis. Within a few days or a week of the onset in cases of acute poliomyelitis, if death has not occurred, it is usual to find rapid recovery in some parts and early atrophy and electrical changes in others. In Landry's paralysis recovery, if it takes place, is slow and evenly distributed, without marked atrophy. (4) In both diseases the sphincters usually escape, the inability to empty the bladder and rectum, which is often a temporary symptom, being due to the impaired abdominal musculature and the position of the patient.

There are several important points to remember in discriminating



between Landry's paralysis and *acute toxic polyneuritis*. (1) Constitutional—Although the constitutional symptoms in Landry's paralysis may be only of slight severity, it is the rule to find some rise of temperature and associated anorexia. Cases of acute toxic polyneuritis may run their course with no corresponding features, unless they depend upon some infective disease, such as influenza. (2) Sensory Phenomena—Reference has already been made to those of Landry's paralysis. In acute toxic neuritis numbness, pins and needles, and sharp pains are common in the extremities, and very definite tenderness of muscles, sometimes of nerves, is the rule. There may or may not be relative anaesthesia in the glove and stocking areas. (3) Motor Phenomena—These are very important, and can only be properly appreciated by carefully and systematically testing the various muscular groups. In the first place, the limbs are more affected than the trunk, and the peripheral parts of the limbs more than the proximal, in acute toxic polyneuritis. Atrophy and electrical changes, perhaps only slight, quickly make their appearance, especially in the dorsi-flexors of the ankles and extensors of the wrists. In the same disease, although other trunk muscles may be attacked, the most marked incidence is generally upon the diaphragm, in which case respiration becomes entirely costal. Of the cranial nerves, those supplying the facial muscles are often picked out and may be the only ones to suffer. Occasionally the palatal or ocular muscles are affected. In Landry's paralysis the musculature is affected generally and evenly, the trunk and limbs presenting a degree of paresis which is more or less symmetrical and equal. In cases in which the paralysis first affects the lower extremities it is not uncommon to find these parts most paretic at the time of observation, but the spread of the disease will then be progressive in an upward direction, and the thoracic muscles may succumb before the diaphragm, or both may be equally weak. When the muscles supplied by the cranial nerves are involved, deglutition, phonation, articulation, and more rarely the movements of the face and jaws, may be impaired, but the fatal termination generally takes place before any of these actions is abolished. The condition may be progressive over two, three, or more weeks, and yet be unassociated with any definite local atrophy of muscles, and recovery may take place without its appearance in any degree of severity. (4) The deep reflexes are abolished in both diseases in the affected parts. The abdominal reflexes are often retained in acute toxic polyneuritis, and are nearly always absent in Landry's paralysis. The plantar reflexes are absent or flexor in type in both instances, and the sphincters are only temporarily, if at all, disturbed. In addition, relapses and recurrences are not infrequent in toxic polyneuritis, whereas they are extremely rare or unknown in poliomyelitis and Landry's paralysis. The accompanying table summarises these points:—

[TABLE



	Landry's Paralysis.	Acute Ascending Myelitis.	Acute Poliomyelitis.	Acute Toxic Polyneuritis.
Temperature .	99°-101° F.	100°-103° F.	102°-104° F.	98°-99° F.
Constitutional.	No constitutional symptoms of importance.	Corresponding anorexia, etc.	Vomiting; anorexia; rigors; convulsions in children.	No disturbance of general health in many cases.
Sensory .	Early paraesthesias. Very little or no sensory loss. Little pain or tenderness.	Profound sensory loss progressing with motor palsy.	Acute pains in back and limbs <i>much increased</i> by passive movement. No sensory loss.	Pains in limbs. Tenderness of nerves and muscles. Relative sensory loss in glove and stocking areas. Sometimes no loss.
Motor .	Progressive symmetrical and even distribution of palsy over trunk and limbs. No atrophy or electrical changes until very late.	Progressive symmetrical palsy spreading from one segmental area of innervation to another.	General palsy at first, but escape of muscles here and there soon noticed. Early atrophy and electrical changes in some muscles.	Peripheral limb muscles more affected than proximal. In the trunk diaphragm suffers before the other muscles.
Cranial nerves .	Partial affection of deglutition, articulation, and phonation if life is prolonged.	Often not affected. Sometimes difficulty in swallowing and articulation.	Occasional affection of one facial, or one ocular, or one glossal muscle.	Double facial palsy (complete) frequent. Ocular and palatal muscles sometimes affected.
Prognosis .	Very grave, but if recovery takes place it is often complete and permanent.	Very grave, but not hopeless. Trophic and bladder troubles are complications.	As regards life depending on respiratory embarrassment. As regards complete recovery very bad.	Fairly good as regards life and recovery, although the liability to relapse and recurrence must be remembered.

**Treatment.**—No therapeutical measures are known to have any definite influence on the course of Landry's paralysis, and none are likely to be efficient until more is discovered about the etiology of the disease. The patient must be placed at complete rest, the head slightly raised, and changes of posture allowed for the sake of his comfort. The bladder may require catheterisation in the first day or two. A purge should be given, and if there is any fever a diaphoretic mixture. Every effort must be made to prevent the production of bronchial catarrh by exposure

to cold, and the administration of atropine or belladonna, together with strychnine, may relieve the respiratory distress by diminishing bronchial secretion when the intercostal muscles and diaphragm become involved. Oxygen and artificial respiration may prolong life, although the necessity for their use generally indicates that a fatal termination is impending. Ergot has been tried, but has generally proved useless. An attempt should be made to discover the micro-organism responsible for the disease; at least 10 c.c. of venous blood should be withdrawn, and lumbar puncture should be performed for bacteriological investigation.

No active treatment of the paralysed parts is indicated until the dangerous stage has passed and the disease has definitely taken a favourable course. Massage and electricity may then hasten the recovery of power. Passive movements should also be carried out daily in order to prevent arthritic adhesions.

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#### HAEMATOMYELIA

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PRIMARY hæmorrhage into the spinal cord is not common, and it is only of late years, by the careful observation and publication of cases with necropsy, that its existence has been fully demonstrated. Charcot and Hayem considered that all the cases were secondary to a primary myelitis; since that time, however, accumulated evidence has placed the occurrence of primary hæmorrhage into the spinal cord beyond doubt.

The rarity of spinal hæmorrhage, as compared with cerebral hæmorrhage, is accounted for thus:—first, the vessels of the spinal cord, even if diseased, are not exposed to the same pressure as the cerebral vessels; and, secondly, the greater proportion of the cases are due to trauma.

**Etiology.**—The large majority of the cases arise from injury—Oppenheim says 90 per cent. Such injury may cause fracture or dislocation of the vertebrae, together with haemorrhage into the spinal cord; or it may give rise to haemorrhage into the cord without any actual injury to the bony canal. In all of Mr. Thorburn's cases the haemorrhage occurred at the level of the fourth, fifth, and sixth cervical vertebrae, and he considers it probable that the haemorrhage is usually produced by a partial dislocation with recoil. The mode of injury varies considerably; a fall on the back, a fall in the sitting position, a fall on to the feet, a direct blow on the back, forcible bending forward of the head by a fall when bearing a weight on the shoulders, diving into too shallow water—any of these may give rise to this accident. Injury during labour has been shewn by Schultze and Dr. H. R. Spencer to cause haemorrhage into the cord of the infant.

Excessive muscular exertion, prolonged exposure to cold (Benda, Boinet), suppression of menses (Eichhorst), and diseases of the vessels are the assigned causes; but in a certain number of cases no definite cause can be found.

Haemorrhage may occur secondary to myelitis, from whatever cause arising, into tumours, and into pre-existing cavities in the cord.

Pregnancy, the puerperal period, venereal excess, and haemophilia may be named as remote or contingent causes.

**Age.**—The disease may occur at almost any age; cases are reported in a child at birth, in a child eleven months old, in a child four years old; but the majority of the cases occur between ten and forty.

**Sex.**—The male sex is much more frequently affected than the female. If, however, the cases due to injury be excluded, it is almost as frequent in females as in males.

**Pathology.**—Haemorrhage into the cord may be found under the following conditions:—

(i.) Capillary haemorrhages, also called "accessory," are found scattered throughout the cord after death from asphyxia, tetanus, and infective processes; these, however, do not give rise to any symptoms, and probably do not occur till shortly before death.

(ii.) Haemorrhage occurring in myelitis—(a) a diffuse haemorrhagic condition; (b) a focal haemorrhage. The diffuse haemorrhage is almost certainly due to a primary myelitis; but in the case of a focal haemorrhage it is difficult, and sometimes impossible, to decide which is the primary condition.

(iii.) Haemorrhage may occur into a tumour or pre-existing cavity in the spinal cord.

(iv.) Haemorrhage may occur into a previously healthy cord in two forms—the first in which the haemorrhage ploughs up the cord in a transverse direction and forms a round or oval-shaped haemorrhage; the second in which the haemorrhage, starting generally in the grey matter, but sometimes also in the white, ploughs up the grey matter in a longitudinal direction, forming an elongated haemorrhage. The lines of least resistance to such a haemorrhage would seem to be the grey matter of the

posterior horns, so that in whatever portion of the grey matter the haemorrhage starts it tends to limit itself to the posterior horns at the extremities. This is further borne out by the experiments of Goldscheider and Flatau, who injected the cords of dogs with Berlin blue in various situations and observed the course it took. Briefly stated, the results were as follows:—Injection into (i.) the anterior horns becomes at the extremities limited to the posterior horns and affects the white matter but slightly at the point of injection; (ii.) the lateral portion at the base of the posterior horn is confined almost entirely to the posterior horn, but affects the middle and anterior horns to a slight degree; (iii.) the posterior horns limits itself to the posterior horns; (iv.) the middle zone affects the grey matter of the same and opposite side, leaving the anterior horns less affected; (v.) the lateral horns affects the white matter at the seat of puncture, the grey matter of the lateral horns, and the posterior horns; (vi.) the posterior column remains limited to the posterior column white matter. Mr. Thorburn, however, says that it tends especially to affect the grey matter of the anterior horns and the central canal.

On opening the spinal canal, the spinal cord may not present any abnormal appearance; in other cases the cord may be expanded at the seat of the haemorrhage, and the dark colour of the blood may be apparent through the distended cord substance; it rarely happens that the haemorrhage breaks through the membranes. Transverse section shews a haemorrhage which usually occupies the central part of the cord, around which the surrounding tissue of the cord is softened and yellow, unless the haemorrhage be quite recent, when it is white. In the later stages of the disease, if the haemorrhage has been quite small, all that may be found is a small pigmented scar containing crystals of blood-pigment. In the case of more extensive haemorrhage the result may be the formation of a cyst, and there is the possibility in still more extensive cases that the process of recovery may give rise to a syringomyelia or to a central gliomatosis; this view of the formation of such cavities is held by Langhans, Minor, Schlesinger, and Schultz.

Syphilitic disease of the blood-vessels has been found, and, in one case, rupture of such a vessel caused haemorrhage into the cord (Williamson). Miliary aneurysms have been found in the cord by Griesinger, Liouville, and Hebold, but there is no evidence that they have ever given rise to haemorrhage into the cord.

**Symptoms.**—The most characteristic feature of the disease is its sudden onset with loss of power in the limbs; it is usually attended by severe *pain*, its situation depending on the level of the lesion. In some of the reported cases prodromes have been present—numbness and pain in the limbs—some time before the loss of power. When the lesion occurs in the upper dorsal and lower cervical regions there is a sharp shooting pain passing through the chest and down the arms, the pain being usually localised to the seat of the haemorrhage, and not extending along the whole spine as in meningeal haemorrhage. Haemorrhage most commonly occurs in the cervical region. In 18 cases collected by Wolff,



7 occurred in the cervical region, 1 in the dorsal, 3 in the lumbar region, and 4 in the conus terminalis; in the other cases the haemorrhage was diffuse.

*Motion.*—Loss of power occurs rapidly in one or both arms, together with loss of power in the legs; the muscles are flaccid, there is retention of urine, loss of knee-jerks and of the superficial reflexes generally. Consciousness is usually retained, though occasionally it has been lost for a few minutes after the onset or injury. When the lesion is in the cervical region, myosis of one or both pupils may be present, drooping of the eyelid, and slightly raised temperature on one side of the face as compared with the other. Paralysis of the intercostal muscles will render the respiration entirely diaphragmatic. The pulse may be slow owing to the interruption of accelerator fibres in the cord.

*Sensation.*—Complete anaesthesia to all forms of sensation may exist below the level of the lesion, with a band of hyperaesthesia at the level of the lesion; this is said not to be present in some cases recorded by Mr. Parkin, and he also notes that in testing the sensation from below upwards or from above downwards there is a difference of an interspace in the result. The dissociation of the various forms of sensation may be a marked feature in some cases, tactile sensibility remaining normal, while sensation to heat, cold, and pain is abolished either on both sides below the lesion, or on the opposite side to the paralysed limb, giving rise to a paralysis of the Brown-Séquard type. With regard to the sense of position and the muscle-pain sense, it is found that this is abolished on the same side as the motor paralysis. Minor has published 8 cases of this type, with a necropsy in 1 case, and in this the lesion was at the level of the first lumbar vertebra, and the haemorrhage extended from the conus below to the level of the exit of the spinal accessory above, and affected the left posterior horn and the hinder part of the anterior horn and the commissure. Similar cases have been published by Ross, Lloyd, Thorburn, and others.

*Reflexes.*—It is generally accepted that the condition of the reflexes depends on the seat of the lesion; certainly in a large number of cases the knee-jerks are abolished immediately after the onset, whether the lesion be in the lumbar, dorsal, or cervical region; and it is also certain that in many of the cases the knee-jerks return and become exaggerated, together with spastic rigidity of the legs: on the other hand, there are cases in which the knee-jerks have remained absolutely abolished after an extensive haemorrhage into the grey matter of the cord in the lower cervical region (Thorburn). That the absence or presence of the knee-jerks goes with the preservation or loss of pain sensation as suggested by Dr. Bastian, would seem not to be the case invariably; for in the first case published by Minor there was complete thermo-anaesthesia below the second rib, with flaccid paralysis of the legs, yet the knee-jerks were increased; there was no atrophy of the muscles. The plantar reflex may shew the characteristic extensor response even when all the deep reflexes are abolished. The abdominal reflexes are absent.

*Visceral Symptoms.*—Constipation and retention of urine are the rule during the earlier period of the disease, and give place to incontinence of urine and loss of control over faecal evacuations in the later stages. Priapism is sometimes present, but its absence is frequently noted. Acute abdominal distension may occur.

The *temperature* is not generally raised at the onset, but it rises slightly a few days later; on the other hand, when the lesion is in the cervicæ region, the temperature may be abnormally low; in one case the temperature fell to 77·6° F. at the time of death, and to 82° F. four days before death (Parkin). The phenomena depending on a cervical lesion and also the occurrence of acute abdominal distension have been fully discussed by Dr. Hughlings Jackson.

*Late Symptoms.*—If the patient survive the acute stage of the disease, atrophy of the muscles in the limb or limbs affected, corresponding to the seat of the lesion, takes place. Electrical changes in the direction of the reaction of degeneration manifest themselves. Vasomotor and sensory disturbances are present, the latter taking the form of preservation of tactile sensation and the abolition of the sensibility to heat, cold, and pain. If the lesion has been in the dorsal or cervical region, considerable loss of power in the legs may remain, with spastic rigidity, increased knee-jerks, and ankle-elongus; but without electrical changes, and without marked muscular atrophy.

*Course and Prognosis.*—The disease may be rapidly fatal, owing to the extension of the hæmorrhage in an upward direction; or it may be fatal owing to extension by secondary inflammation occurring two to three days after the actual onset; or to the supervention of bronchitis or pneumonia, the intercostal muscles being paralysed. The patient may, however, recover from the immediate effects of the disease, and succumb to a purulent cystitis or to infection through a bed-sore. In the more favourable cases partial recovery takes place, atrophy of some muscles generally remains, and the rigidity of the legs persists, with increase of knee-jerks and some difficulty in passing urine. The sensory disturbance, and especially the loss of sensibility to heat, cold, and pain, may remain for a long time, if not permanently.

*Diagnosis.*—(a) From *acute myelitis* it is at times impossible to separate either primary hæmorrhage into the cord or hæmorrhage secondary to the *acute myelitis*. In most cases the onset of myelitis is more gradual, attended by more marked prodromes, by a raised temperature, and the gradual extension of the symptoms. That the onset in myelitis may be absolutely sudden is shewn by a case reported by Dr. Williamson (49); pain was, indeed, absent at the onset, but, according to his statement, von Leyden has shewn that it may be absent also in cases of spinal hæmorrhage.

(b) From *hæmorrhage into the spinal membranes* four points may aid in the diagnosis—first, the marked irritation of the nerve-roots, as shewn by the violent pains in the limbs and the jerking of the muscles; secondly (if the lesion be in the cervical region), the paralysis of the upper limbs

is greater than the lower; thirdly, there is not the myosis of the pupil which occurs when the hæmorrhage is into the cord; and fourthly, the dissociated tactile and temperature sense is not present (*vide* p. 592).

(c) The disease is apt to be mistaken for *acute poliomyelitis*, especially in a child; examples of this in an infant of eleven months (Clifford Allbutt) and a child of four years (Cheadle) have been reported (*cf.* p. 628).

(d) From *syringomyelia* and central gliomatosis it may be impossible to distinguish the later results of hæmatomyelia; one point brought forward by Remak may be mentioned, namely, that in gliomatosis the atrophy and the dissociated sensation occur in the same limb, whereas in hæmorrhage the limb on the opposite side to the atrophy is affected with regard to sensation. No proof of the above statement is given, the explanation is not obvious, and it needs further confirmation.

It is most important to differentiate between a hæmorrhage into the spinal membranes and one into the substance of the spinal cord, for in the former condition laminectomy will relieve the pressure, whilst in the latter condition no benefit will result from such an operation. The presence of the Brown-Séquard phenomenon, in which there is motor paresis on one side of the body and dissociated sensation on the opposite side of the body, is strongly in favour of a hæmorrhage within the substance of the spinal cord (*vide* also p. 592). In considering the question of operation, however, the presence of this syndrome should not necessarily negative operation, for complete recovery has followed surgical interference when the syndrome has been present.

**Treatment** consists in absolute rest, the patient being placed in the prone position, with the application of an ice-bag over the seat of the hæmorrhage. The bowels should be freely open, and the retention of urine relieved by the use of the catheter. Ergot should be given by the mouth or subcutaneously. Operation can be of no service in a case of true hæmatomyelia; but since, as the result of injury, hæmorrhage may occur both within and without the spinal cord, it is necessary to consider the advisability of a laminectomy in certain cases which present symptoms pointing to an intra-medullary hæmorrhage. Later the treatment resolves itself into that of the bronchitis and pneumonia, and the prevention of erysitis and bed-sores. The after-treatment consists in the application of electricity, massage, and movements to the affected muscles.

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## CAISSON DISEASE

SYNONYMS.—*Compressed-Air Sickness* ; *Divers' Paralysis*.

By LEONARD HILL, M.B., F.R.S.

THIS disease takes its name from the steel chamber or caisson employed for sinking in water or wet soil in bridge-building, shaft-sinking, and tunnelling; the water is kept out by compressed air. Divers, who also work in compressed air in diving-bells or clothed in diving-dresses, suffer equally with caisson-workers, and the disease is better entitled compressed-air sickness, as the exposure to compressed air has been proved to be the responsible factor. Popularly, the sickness is known among divers as "the Pressure," among caisson-workers as "Bends."

**Etiology.**—It has only become noticeable since the technical improvements in the diving-dress made by Siebe, and the invention of sub-aqueous chambers in the middle of the last century rendered possible extensive aquatic engineering and marine salvage feats. A caisson in its simplest form is a vertical iron cylinder open below and closed at the top by a sliding door, which leads into a smaller chamber or air-lock through which men and material enter or leave the caisson. The caisson is weighted with masses of concrete and made to sink vertically through the water or wet soil; the water is kept out by pumping compressed air in, and the air escapes under the lower or cutting edge of the caisson, and thus ventilation of the chamber is obtained. The men work in



dryness at the bottom, and as they hollow out the soil, so the caisson sinks by its own weight. In tunnelling, a horizontal caisson is used, terminating in a shield which is driven forward by jacks worked by hydraulic pressure; there are doors in the shield through which the soil is removed. As fast as the shield is driven forward, fresh steel segments of the tunnel are set in place and concreted in. By this means tunnels are driven under the rivers of great cities a few feet beneath the river-bed. The workmen, when they enter the air-lock, are "compressed," and when they leave it "decompressed" ("locking in" and "out"). The air-lock is furnished with taps, and when the men enter they close the door to the open air, open the cock in communication with the caisson, and equalise the pressures in the caisson and air-lock, and then open the other door and enter the caisson. On leaving, they reverse the process by opening the cock which communicates with the outside air. The men work in a pressure of air which just exceeds the hydrostatic pressure of that depth of water which extends from the working face of the caisson to the surface. A diving-dress consists of a waterproof suit made of rubber and canvas joined round the shoulders to a rigid helmet in a water-tight fashion. Air is supplied by pumps, and delivered to the helmet through an inlet valve by a long flexible pipe. The air fills the helmet and upper part of the dress about the chest, and escapes into the water through an adjustable outlet valve in the side of the helmet. The air is compressed in the helmet by the pump to a pressure which just exceeds the hydrostatic pressure of the depth of water between the outlet valve and the surface. The diver is "compressed" as he descends by a rope fixed to a sinker on the bottom, and "decompressed" as he ascends. Caisson-workers are usually exposed to a lower total pressure than divers, but they work for longer shifts. In both cases serious illness and death have been, and still are, frequent. The following are some caisson-sickness statistics: Douchy Mines, 63 cases; Kehler Bridge, 133 cases; St. Louis Bridge, 119 cases out of 352 workers (50 cases of paralysis with 14 deaths); Brooklyn Bridge, 110 cases, 3 deaths; Tonlon Dry-Dock, 43 cases, 2 deaths; Coulsac Bridge, 104 cases, 3 deaths; Eisler Bridge, 38 cases, 2 deaths; Nussdorf, 320 cases out of 675 workers; Felesti Bridge, 55 cases and 5 deaths out of 154 workers; Hudson River Tunnel, 3 deaths a month until conditions were improved; lately 16 deaths out of 10,000 exposures to compressed air.

Few caissons are worked above + 30 to 35 lbs.,<sup>1</sup> though the pressure has been as high as + 45 lbs. and even + 50 lbs. in some (St. Louis). The shifts are usually six to eight hours at the lower, and two to three hours at the higher pressures (one hour at + 50 lbs. in America). Divers frequently go down to 20 fathoms (120 ft. = + 53 lbs.) or more, but stop a few minutes only at great depths. Experience has shewn that the higher

<sup>1</sup> Each 33 feet of sea water ( $5\frac{1}{2}$  fathoms) or 34 feet of fresh water equals the pressure of one atmosphere, 14.7 lbs. to the square inch, roughly 15 lbs. A depth of 66 feet equals a pressure of 2 atmospheres positive or 3 atmospheres absolute, or + 30 lbs. The record depth attained by divers is 210 feet.

the pressure, the longer the shift, and the shorter the period of decompression, the greater is the risk; that the illness occurs only after "decompression," and may not come on for some minutes, or even half an hour, after the worker has been decompressed; that old men, and men of heavy build and fat, are more susceptible than young men of spare frame; that recompression is the best method of treating the illness and alleviating the symptoms. It is important to remember that caisson-workers may be poisoned by carbon monoxide, or come under other dangers incidental to subterranean workers, which have nothing to do with compressed air. Compressed-air sickness is characterised by the fact that it occurs only after decompression; the only damage which can occur during compression is to the membrana tympani from non-equalisation of the air-pressure in the middle ear and outside, owing to closure of the Eustachian tube by catarrh; acute pain may then be produced, and the membrane even be torn or haemorrhages occur in the middle ear. The accident occurs during the rise of the first few pounds of pressure, when the alteration of the volume of air in the ear is greatest. Men with catarrh should not enter the air-lock. As the opening of the Eustachian tube is valvular outwards, decompression causes no trouble. The Eustachian tube can generally be opened by swallowing, by a forced expiration with closed mouth and nose, and by yawning. Practised men can be compressed to + 30 lbs. in about a minute without trouble from this cause. Bad conditions in the caisson, such as hot moist air, over-fatigue, impurities from the soil, such as  $H_2S$  or CO from furnaces, may by weakening the men contribute to the risks of compressed air. Thus, at the King Edward VII. Bridge, Newcastle-on-Tyne, several men were affected when the caisson was passing through a stratum of soft mushy coal of unpleasant odour, although the air-pressure was quite low.

Candles and tobacco are consumed with fury in compressed air; a candle blown out relights itself, a cigarette flames with each puff. The living body, on the other hand, is able to regulate the pace of its combustion, and cannot be fanned merely by an increased oxygen-supply into an increased rate of combustion. The increase in the partial pressure of the oxygen within limits has a favourable action. Whereas breathing oxygen up to 90 per cent of an atmosphere (= air at + 50 lbs.) has no effect on the metabolism of the resting man, it increases the power of the athlete or worker, as I have shewn, in great exertion, for the oxygen use then runs beyond the supply. It is certain, therefore, that navvies perform heavy work more easily in compressed air. The fall of oxygen-pressure during decompression is a disadvantage to the heart of the navvy tired after his labour. Beyond a certain limit, an increase of oxygen-pressure is poisonous. It has a convulsant action (Bert), and produces congestion and even consolidation of the lungs, with all the signs of an acute pneumonia (Lorrain Smith, Hill). The time of exposure and the partial pressure of oxygen are the two important factors; a partial pressure of oxygen equal to 80 per cent of an atmosphere produced pneumonia in mice in four days, 125 per cent in three days,

180 per cent in twenty-four hours, and 300 per cent in five hours (Lorrain Smith). Larger animals are affected in about the same time (Hill and Macleod). Highly compressed air causes rapid toxic effects in proportion to the partial pressure of oxygen (Bert, Hill). The limit of safety for short exposures, as far as concerns oxygen, is 10 atmospheres or 300 feet of water. No diver has ever reached this depth owing to the much greater dangers of decompression. The evidence drawn from the Siebe-Gorman life-saving dress used in mines, etc., for rescue work, is conclusive that it is not only safe for a man to breathe almost pure oxygen for two to six hours at a time, but that this does not produce any ill effects. The ordinary method of giving oxygen to patients, with an open funnel, does not give a percentage of oxygen in the alveolar air higher than 20 to 25 per cent. By employing a face-cover, over 70 per cent may be obtained. The writer makes a suitable mask of a square of thin waterproofing with a celluloid face-piece let into it. An elastic band confines the upper part of the square round the forehead, the lower part is tucked into the neck collar. The oxygen pipe is let into the mask opposite the mouth, and a current is used sufficient to blow away the expired  $\text{CO}_2$ .

**Pathology.**—The majority of medical writers on this subject have supposed that exposure to compressed air mechanically altered the distribution of the blood, forced it inwards, and produced congestion of the viscera and central nervous system, with consequent sudden and dangerous reflux on decompression. It is only a failure to appreciate the elementary principles of physics which has given rise to these conceptions. The air-pressure is transmitted instantaneously throughout the fluid mass of the tissues, and equally in all directions. If it were not so, we could not bear even the ordinary changes of barometric pressure. How little pressure *per se* affects protoplasm is shewn by the fact that living forms are dredged from even the greatest depths of the sea, from abysses 5 miles deep, where the pressure of the water is measured by hundreds of atmospheres. It need scarcely be said that striking effects are produced by exposure of different parts of the body to unequal pressure, as is seen in cupping. If the air-pressure in the lungs exceeds the pressure on the surface of the body by only a few inches of water, air may be forced into the circulation, and it is said there is a risk of this happening in the forcible blowing of wind instruments. If a diver fall through the water so quickly that the pump cannot keep up with him, and the air-pressure in his helmet becomes less than the pressure of the water on his body, then pulmonary, nasal, or conjunctival hæmorrhages may occur. The difference of pressure makes the helmet act as a large cupping-glass. It is unsafe, therefore, for the diver to let himself drop down to the bottom of deep water; he must go down the shotted rope, and it is quite safe for him to do this quickly, for example, at the rate of 200 feet in two minutes. A most powerful but very risky way of profoundly affecting the circulation is to breathe air at a pressure different to that to which the body is exposed.



Hoppe-Seyler in 1857 and Bucquoy in 1861 independently put forward the correct solution of the startling cases which were then attracting notice owing to the use of caissons by Triger in the sinking of certain French coal-mines on the banks of the Loire. "During and after decompression," wrote Bucquoy, "all the gas dissolved in the blood, owing to the condensation of the air, tends to escape from the liquid with efforts so much the greater, for equal times of exposure, the greater the pressure to which the subject has been submitted. This is a necessary consequence of the physical laws of the solution of gases in liquids, and we have a familiar and common illustration in the rapidity and force with which carbonic acid escapes from an aerated water when the bottle is uncorked." Paul Bert, by the patient and accurate use of the experimental method, proved that the extra nitrogen which is dissolved in the body while under pressure is given off as bubbles within the body when the pressure is suddenly reduced, and that the excess naturally finds its way out through the lungs by diffusion, and no bubbles or symptoms arise if the decompression be made gradually enough. As the bubbles are given off in the fluids of the body, and particularly in the blood, it may easily be imagined that almost any kind of symptoms may arise. Thus, there has been chronicled a sudden loss of sight arising from a bubble in the central artery of the retina, aphasia, dementia from blockage of cerebral arteries (Catsaras). Of the more frequent and graver symptoms, dyspnoea or death are due to pulmonary air-embolism or embolism of the coronary vessels, paralysis to blocking of the vessels of the spinal cord. The commonest symptom in caisson-workers and the least grave is more or less severe pain about the joints. The crackling of bubbles in the fasciae and aponeuroses has been felt in some of these cases. The probable explanation is the stretching of a small nerve-twigg by bubbles occurring in dense, inextensible structures, such as aponeuroses and ligaments, or possibly in nerve-sheaths. The more severe "bends" are very probably caused by bubbles in the spinal cord. Caisson-workers are far more liable to these "bends" than divers, because they saturate the parts with nitrogen by the rapid circulation which pertains during heavy muscular labour, and then sit quiet with a fatigued heart and far slower circulation in these parts during decompression.

Bubbles of gas found set free in the blood of the heart have been shewn to contain about 82 per cent  $N_2$ , 16 per cent  $CO_2$ , and 2 per cent  $O_2$ . The last two gases are set free from their loose chemical combination with the blood because the nitrogen-bubbles act as a vacuum chamber in respect to these gases. As the circulation becomes blocked by the bubbles the venosity increases, and this results in the high proportion of  $CO_2$  and low  $O_2$  value. Nitrogen dissolves in the water of the body to the extent of 0.9 per cent for each atmosphere at body temperature. In the watery part of a man weighing 60 kilos there are about 540 c.c.  $N_2$ ; at + 15 lbs., if saturated by a long enough exposure, 1080 c.c.; at + 75 lbs., 3240 c.c. Dr. H. M. Vernon has shewn that fat dissolves more than five times as much  $N_2$  or  $O_2$  as water. Thus, an animal with 25



per cent fat takes up twice as much  $N_2$  as one with no fat. Hence fat men must be excluded from compressed-air work, and lean wiry men chosen. An average man contains 15 to 20 per cent of fat, and a man of 60 kilos, with 15 per cent fat, would contain about 970 c.c.  $N_2$  at 1 atmosphere; 1940 c.c., if saturated, at + 15 lbs.; 2910 c.c. at + 30 lbs.; 3880 c.c. at + 45 lbs.; 4850 c.c. at + 60 lbs.; and 5820 c.c. at + 75 lbs. Supposing the man were killed at + 75 lbs. and decompressed, some five litres of nitrogen would be set free in his body. The dissolved oxygen combines chemically with the tissues and blood, and does not contribute to "bubble" formation.

During compression the blood passing through the lungs becomes saturated with  $N_2$  according to the pressure of  $N_2$  in the alveolar air. The blood carries the nitrogen to the tissues and shares it with these, and returns to the lungs for more. This goes on till the whole body is saturated. The process obviously is a slow one, as the blood is the carrier, and must be particularly slow in places where the circulation is very sluggish. The mass of blood is about 5 per cent of the body, and the capacity of the tissues to dissolve  $N_2$  is estimated by Dr. Boycott at thirty-five times that of the blood; in a fat man considerably more, if the blood were fully saturated in the lungs and desaturated in the tissues. If the blood were evenly distributed and circulated at an even rate throughout the body, postulates which are probably far from the case,  $\frac{1}{35}$  of the total amount of nitrogen required to saturate the tissues would be taken up after the first complete round of the whole blood,  $\frac{1}{35}$  of  $\frac{34}{5}$  of the total after the second round, and so on (v. Schrötter). In twenty-three rounds the body would be  $\frac{1}{2}$  saturated, and in ninety-two rounds  $\frac{15}{16}$  saturated. Suppose the whole blood completes the circulation in one minute, minutes can replace rounds in the above. Experimenting on ourselves, Mr. Greenwood and I found that the urine excreted during profuse diuresis was saturated with  $N_2$  in ten to fifteen minutes. Other parts of the body have a far slower circulation than the active kidneys, and must saturate at a far slower rate. Muscular work has a most profound effect on the rate of circulation and on the rate of saturation. Nothing could be more unfavourable than the habit of the caisson-worker who saturates his body by hard work, and then rests during decompression, fatigued after his labour, with a tired heart and slow respiration.

The principles which govern the escape are the reverse of those which rule the saturation. The blood gives up  $N_2$  to the alveolar air, and returns to the tissues for more. Those organs in which the circulation is rapid will yield up their  $N_2$  quickly, and those with a sluggish circulation slowly. As the pressure falls the carrying power of the blood falls with it, and at the end of decompression a condition may be set up in which the slow tissues still hold, say, 3 per cent  $N_2$ , while the blood can dissolve only 1 per cent. Herein we have the danger of bubbles forming. Bubbles form much more easily in water than in thick colloidal or viscous solutions such as blood, they likewise run together and escape from water far more easily. Contrast air-bubbles shaken up in treacle and in water.

Albumin may be detected by the persistence of the froth when urine is diluted and shaken. Super-saturated solutions may not give off any bubbles if there are no points, such as dust particles and rough surfaces, on which the bubbles can form. In animals killed by rapid decompression we find bubbles in the blood, in the fat areolar tissue, gas in the stomach and bowel, and in the peritoneal cavity. There are, as a rule, no, or only few, bubbles in the urine within the bladder, in the gall, aqueous humour, or amniotic fluid. The urine and amniotic fluid when spilt bubble freely. There are evidently certain physical differences, as yet unstudied, which lead to the liberation of bubbles in the blood-vessels, and not in the bladder. There are also differences between one individual and another, so that in caisson-sickness one man is taken and another left, and a rate of decompression found safe for the majority is fatal for the few. Such differences are due probably to varying susceptibility to fatigue on the part of the circulation rather than to varying tendency to bubble formation. Obstruction of the circulation due to flatulent distension of the intestines is an important contributory cause in goats (Hill and Greenwood). Experience shews that the men who work the lock gates, and are frequently compressed and decompressed, do not suffer; that officials and visitors, who stay but a short time and do no work, do not suffer; that the longer the working hours, the greater is the amount of illness; that no illness occurs with low pressures, *i.e.* less than + 18 lbs. That the safest desaturation of the body depends on the activity of the circulation and rate of respiratory exchange is shewn by experiments on small and large animals. The activity of the circulation is proportional to the rate of respiratory exchange per kilo of body weight, and that is proportional to the surface of the animal. Mice and small rats survive decompression in a few seconds from + 100 lbs., whilst large rats, and particularly pregnant rats, are killed. The nitrogen escapes easily into the peritoneal cavity in these small animals. Dr. Boycott found the death-rate in rats varied as their fatness; out of twenty-nine rats the fat in those that died averaged 4.5 per cent, and in the survivors 2.8 per cent. Rabbits are killed by a rate of decompression which rats survive. When we come to the bigger animals, the relative difference in weight and death-rate becomes less marked. If its circulation is depressed during the compression period by the administration of an anaesthetic, the small animal becomes more susceptible, and this points to the danger to man of exhausting himself while under compression. The individual susceptibility in a series of animals of equal weight, age, and fatness is very well marked, and depends on factors which have not yet been ascertained. In caisson-works if 1 per cent of the workers are killed, about 50 per cent will go through months of work without any illness. Whilst no immunity is established by work in compressed air, some individuals, who are undoubtedly very susceptible, should be weeded out by trial work at low pressures before proceeding to higher ones. Dr. Boycott, from a few observations on goats, suggests that the susceptible individuals have a lower rate of respiratory exchange. Their intestinal flatulence is, I think, a far more potent factor.

Chance largely determines the position where the air-bubbles form, whether after their formation they are swept on by muscular exertion into dangerous parts. The bubbles are for the most part set free in the venous blood. After decompression in five seconds from 100 lbs. I have found evidence of bubbles in the cells of the liver and kidneys of cats. The histological appearance suggests that the gas is set free from the fat in the cells. No bubbles form in the tissue-cells under slower rates of decompression. The bubbles may pass through the lungs in their finest form, and enter or actually form in the arteries. The fat, owing to its high coefficient of absorption for  $N_2$ , is a place where air-emboli form, and this is of particular importance in regard to the white matter of the spinal cord. A small bubble lodging in a capillary of the spinal cord probably grows by accretion of the gas dissolved in the myelin. The poor blood-supply of the white matter favours this, and thus air-emboli and consequent softenings are far more common in the white than in the grey matter. Hence paraplegia is one of the commonest of the severe symptoms of caisson-sickness. In goats many bubbles and patches of softening have been found in the cord, and sometimes there were few symptoms to denote their presence. In some goats hundreds of bubbles were counted in the cord, and there were five times as many in the white as in the grey matter. In one goat, which was compressed seventeen times and had temporary paralysis twice and "bends" four times, 103 bubbles were counted in sections of the lower dorsal and upper lumbar cord, and patches of necrosis were found in the lateral column at the level of the fifth dorsal and in the posterior column at the level of the fourth lumbar root (Boycott and Damant). There can be little doubt that workers often have bubbles in them after decompression without any symptoms. In all the fatal cases of divers' palsy submitted to careful necropsies patches of necrosis and secondary degenerations in the cord have been found.

The symptoms were described in the first edition of this work by Dr. Andrew Smith thus:—"In the order of frequency: pain, often very severe, in one or more of the extremities, and occasionally in the trunk; pain in the epigastrium, which may or may not be associated with nausea and vomiting; paralysis, more or less extensive and complete; headache; vertigo, and coma. In rare cases sudden death occurs almost without preceding symptoms. The pain, which is of a neuralgic character, may be slight and transient, or extremely severe and persistent. It is usually intermittent or remittent. It may come on gradually, increasing in severity until it becomes absolutely intolerable; or it may begin at once in its full intensity. The knees, legs, and hips are most frequently attacked; but the arms or trunk may be the first to suffer. Sometimes the greatest suffering is in the back, and particularly in the lumbar region. Epigastric pain is frequent; if not quickly relieved, it is followed by sickness and vomiting. Vomiting may take place without preceding gastric pain, and then is usually accompanied by giddiness or other evidence of cerebral origin.



"Paralysis occurs with increasing frequency and completeness in proportion to the degree of pressure and the duration of the exposure to its influence. The lower portion of the body is more liable to attack, but the upper extremities are not exempt. The paralysis is of sensation as well as of motion, but it gives no relief to the pain. The part is insensible to pinching or to the prick of a pin, while at the same time it is the seat of extreme suffering. But there is no necessary relation between the pain and the paralysis, as either may occur separately. The paralysis varies in degree, from a slight and transient paresis with some impairment of sensation to complete and permanent loss of motion and sensation in the affected part. Even the minor degrees usually include the bladder.

"Symptoms indicating cerebral disturbance of a transient character are often observed, such as headache, double vision, giddiness, incoherence of speech, and occasionally syncope. The skin is often mottled in patches, some of which are veritable ecchymoses; others are the result of stasis in the distended capillaries, and can be rubbed away by persistent friction.

"The *duration* of an attack varies extremely. It may last a few hours, or it may continue for six or eight days. Paralysis may be recovered from in a few days, or be protracted for weeks or months. Death occurs only in cases that are severe from the first; and, except when due to secondary lesions, it usually takes place shortly after the attack." The following is the description of a typical fatal case:—

A man of thirty-three, exceptionally strong and in good health, descended 24½ fathoms in search of a torpedo, being therefore exposed to a positive pressure of between 4 and 5 atmospheres. He remained below forty minutes, and ascended in half that time. He entered the boat without any trouble, and when the helmet was removed, chatted unconcernedly about his work. He had suffered no inconvenience in the water, and only returned because the light was insufficient for his purpose; his comrades agree that he had never before come up in better condition. All was well for some eight or nine minutes, when suddenly he experienced pains in the stomach, and asked the attendants to get his dress off quickly, as he wished to go on board. In a few seconds he said, "Send for the doctor," and immediately collapsed. Fleet-Surgeon M'Kinlay, who was in attendance at once, found the man cyanosed and breathing stertorously, the lips covered with foam; he was undressed, but expired fifteen minutes after gaining the surface, and six or seven counting from the first symptoms.

At the necropsy the surface of the brain was deeply engorged with dark fluid blood; many air-bubbles were detected in the veins of Galen and choroid plexus, also in the superficial cerebral vessels when the latter had been partly emptied of blood. The veins on the surface of the heart were beaded with air, and that organ felt like a bladder half full of water, gurgling loudly when pressed. On incision of the right ventricle air escaped with a puff; the left ventricle was empty. The mesenteric vessels were likewise filled with air, and the liver frothed on section (M'Kinlay).

In its sudden onset, rapid termination, and morbid changes, this case



gives a more harmonious picture than an exhaustive catalogue of the symptoms recorded by different observers.

**Prevention.**—It has been the custom to decompress workers far too quickly and without any definite plan. Where regulations have been established for carrying out the decompression in a time all too short, the workmen have generally contravened the rules and let themselves out of the lock quickly. The difficulty of making the men conform and the expense have prevented the application of the knowledge, gained by Bert and others, that if the time of decompression of animals is prolonged to about an hour, there is little risk of serious mischief. If the period of their compression is made very short, say fifteen minutes at + 45 lbs. and two minutes at + 75 lbs., divers can and do return safely and rapidly to the surface. At the St. Louis tunnel (+ 45 lbs.) a high death-rate was abolished by reducing the shift and extending the decompression period. It seems probable that the reduction was effective not so much by lessening the saturation, for the body of a man doing hard work must be fairly saturated in two hours, as by stopping the fatigue of the heart.

Divers not seldom go to double the pressures employed in caissons, because they stay down but a short time, *e.g.* in sponging, pearling, or seeking for lost gear.

There is no question that serious accidents can be prevented by working out suitable lengths of compression and decompression. If the tissues were gradually and uniformly saturated it would be natural to suppose that they should be uniformly and gradually desaturated, and most authors following Bert have advocated a uniform system of decompression extending up to twenty minutes per atmosphere (*v. Schrötter*). Drs. Haldane and Boycott, dwelling on the fact that there are tissues which saturate quickly and others which saturate slowly, have elaborated for the use of Admiralty divers a set of tables giving times of compression, short enough in their opinion to prevent saturation of the slow tissues, and introducing a system of stage decompression. The Admiralty divers are now decompressed rapidly to some half the full pressure, and are decompressed the rest of the way in stages which get longer the nearer the pressure falls to zero. For example, if a diver has been working at a depth of 144 feet for a period not exceeding ninety minutes, he ascends rapidly to 50 feet, then pauses ten minutes; next comes to 40 feet, and waits ten minutes; at 30 feet he stops twenty minutes; at 20 feet, thirty minutes; at 10 feet, thirty-five minutes, and then leaves the water. From a number of experiments on goats, Drs. Haldane and Boycott conclude that the absolute pressure can be rapidly reduced to one-half without risk. Thus, they say, a man at + 75 lbs. (90 absolute) can be safely decompressed in three to four minutes to + 30 lbs. (45 absolute), and from + 45 lbs. (60 absolute) to + 15 lbs. (30 absolute). Stage decompression, by establishing a big difference of  $N_2$  pressure between tissues and atmosphere, urges the nitrogen out of the body. Bubbles do not form easily in viscous solutions, and either are not formed at all during the quick drop from say + 75 to

+ 30 lbs., or are kept too small at the latter pressure to do any harm. The tissues and blood will be supersaturated, and the supersaturated blood coming to the lung will yield up its nitrogen if time enough be given in the later stages without formation of bubbles. In agreement with these theoretical considerations, Drs. Haldane and Boycott find a stage decompression of goats is far safer than a uniform, the same total time being spent in both cases. Mr. M. Greenwood, jun., and I have successfully decompressed ourselves from pressures up to 75 lbs., and in one case 92 lbs., by the uniform method of twenty minutes per atmosphere. This was after short exposures at these high pressures, and after exposures of an hour or so to pressures above 50 lbs. We have not been able to confirm on pigs Haldane and Boycott's results; these have a bodily formation (and in particular an alimentary canal and contents) far more like that of man than a goat's. The distension with fermentation gas of the enormous bowels of the goat on decompression complicates the problem. This distension obstructs the circulation. Some of our goats died from obstruction of the bowels due to the enormous gaseous distension of the stomach, two to three days after they had been decompressed. In a hundred experiments the statistics shew that Haldane and Boycott's stage method is less safe for pigs than the uniform method, and neither are trustworthy. We obtained much better results with a continuous decompression, but one getting slower and slower as the pressure falls. This was obtained by opening the tap a certain amount and leaving it at that amount, so that the pressure dropped, say, from + 75 to + 60 in the first five minutes, and from + 15 to + 0 in the last forty minutes.

Finally we have worked out a method which is safe. We have proved that water exposed to + 90 lbs. till saturated, does not bubble when reduced rapidly to + 20 lbs, and only gives off very fine and most minute bubbles when violently shaken at + 20 lbs. The resistance to the formation of bubbles is very great, and a pressure of + 20 lbs. is sufficient to prevent their formation. If the water is gently shaken for some time at + 20 lbs. the excess of dissolved air comes off without bubbling. In eighty experiments on pigs, some very fat (50-115 lbs. in weight), we have decompressed them, after two hours' exposure to + 75 to + 90 lbs., and having lowered the pressure to + 20 lbs. in 10 minutes, kept them at + 20 lbs. for 90 to 120 minutes (the longer time for the heavier pigs) and then brought them to + 0 in 10 minutes. This method has reduced our accidents to 2 per cent; and for men wiry, thin, young, who can exercise themselves during decompression and breathe deeply, the accidents would probably be nil. Breathing oxygen between the periods of exercise would help.

In caisson-works a comfortable lock must be arranged at 18 to 20 lbs. pressure, and the men be kept in this an adequate time before returning to the outside air. For high pressures the shifts must be short, say two hours, so as not to fatigue the heart. Flatulence is a contra-indication.

**Treatment.**—The sovereign cure for symptoms is immediate recom-

pression. The early caisson-workers found this out for themselves, and Foley (1863) recommends it. Dr. Andrew Smith established a medical air-lock at Brooklyn Bridge, into which sufferers were put, and Mr. E. Moir advocated and made great practical use of such a lock in the Hudson Tunnel works. A medical lock is now supplied at all works, and should be provided on board any salvage-ship engaged in deep-diving work. Divers can be kept in their clothes with the helmet off for some little time after a deep job, and be sent down some 50 feet if affected with any symptoms. By recompression the bubbles are greatly diminished in size or redissolved. Decompression must be carried out very cautiously in order to prevent recurrence of the symptoms, for the bubbles when once formed are not easily got rid of. We have relieved pigs from severe dyspnoea by recompression to +18 lbs., but the symptoms have returned on decompression half an hour later.

The following is a typical case for which I am indebted to Mr. E. Moir:—

A. M. has worked steadily for weeks after being passed as medically fit. Worked October 8 for six hours at +34 lbs. Decompressed at 4 p.m. After going home at 4.45 p.m. began to have severe pains all over and weakness. Became much worse, unconscious, blue, bathed in sweat, pulse almost imperceptible, stopping breathing for two minutes, appeared to be dying. Ambulance surgeon at first refused to remove him, but was persuaded to bring patient to air-lock; at 5.15 p.m. recompressed. As no improvement was apparent at +30 lbs. the pressure gradually reduced. Massage kept up all the time. Began to improve, so at 6 p.m. pressure raised from +15 lbs. to +34 lbs. His condition at 6.30 p.m. was—colour fair; pulse 60, irregular; respirations, 28; conscious and answered questions, could raise up body, but very weak. As pressure gradually came down, he seemed to improve very slowly; his colour was better, his pains gradually left, and he was brighter. Considerable stimulation and massage was kept up throughout the whole period of decompression. Blotches on skin became marked at one period. Came out of pressure at 11 p.m. Wholly conscious, able to sit up with difficulty, colour good, no sweating, pulse still weak, 120; heart and lungs normal, abdomen very tender but not rigid or distended, blotches fainter. On October 12 he came to work to be paid off.

This man was saved by the recompression and very slow decompression lasting six hours.

Caisson-workers ought to sleep and live in barraeks close to the medical lock, so as to be near aid during the first hour after decompression. Muscular movements or massage and oxygen-inhalations can be used during decompression. Apart from recompression little can be done. Mere massage of the sick man may move the bubbles on from a dangerous part, but is as likely to move them into a dangerous part. "Bends" can be treated by friction and fomentation, but recompression is the sovereign remedy, only it must be administered early. Paralysis, when once established, can only be treated on the ordinary palliative lines. Great care must be taken to prevent malingerers obtaining



compensation on false pretences. I have met a man sharp enough to study the symptoms and simulate the sickness.

LEONARD HILL.

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(A complete bibliography up to 1900 will be found in the treatise of v. Schrötter, Heller, and Mager.)

L. H.



## MOTOR NEURON DISEASE

## PROGRESSIVE MUSCULAR ATROPHY OF NEUROPATHIC ORIGIN

By the late C. E. BEEVOR, M.D., F.R.C.P.

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UNDER this heading the conditions known as poliomyelitis anterior chronica, amyotrophic lateral sclerosis, and progressive bulbar paralysis will be described. There has been much discussion as to the distinction of these various forms of disease, but the weight of evidence, both clinical and pathological, is strongly in favour of placing them in a single group. It is difficult to find a perfectly suitable designation for the various symptoms which may be caused by primary degeneration of the upper and lower motor neurons. The conception of the disease should be a primary degeneration of both upper and lower motor neurons. It is then easy to realise that the clinical picture may vary greatly—*first*, according as either upper or lower neurons are first effected; *secondly*, according to the group of lower motor neurons primarily affected.

**History.**—In 1850 Aran described 11 cases of muscular atrophy, and noted that the small muscles of the hand were first attacked. In 1853 Duchenne's memoir on these cases appeared, and in the same year Cruveilhier published 3 cases with necropsies, in 1 of which atrophy of the anterior roots was found. In 1859 Duménil recorded a case of glosso-labio-laryngeal paralysis with atrophy of the hypoglossal nerve, which he regarded as a form of progressive muscular atrophy. In 1860 Duchenne described other cases, but he regarded his cases as quite different, for he says that in glosso-labio-laryngeal paralysis there is paralysis without atrophy, whilst progressive muscular atrophy is a lesion of muscular nutrition without paralysis. From the account of the tongue in his case there can be little doubt that there was considerable atrophy. In 1867 Lockhart Clarke first found diminution in size and change in the cells of the anterior horns.

In 1872 Chareot described the condition of amyotrophic lateral sclerosis, and shewed that there was sclerosis of the lateral columns of the spinal cord, in addition to atrophy of the cells of the anterior horns. The patients presented rigidity of the limbs and increase of the deep reflexes which preceded the muscular atrophy. He regarded the atrophy of the cells as secondary to the lateral sclerosis, and hence called these cases deuteropathic, in contra-distinction to the protopathic cases of progressive muscular atrophy. Modern methods of pathological investigation, especially those of Marchi and Nissl, have shewn that in a large majority of cases there is a degeneration of both the upper and lower motor neurons, although the relative affection of these two systems

may vary considerably in individual cases. That cases of toxic degeneration of the lower motor neurons, both acute and chronic, exist, in which there is no evidence of affection of the upper motor neurons, is certain. These cases do not, as a rule, follow the distribution or course seen in progressive muscular atrophy, and have been described by Dr. A. S. Barnes and others under the title, "Toxic Degeneration of the Lower Motor Neuron" (*vide* p. 459). Oppenheim still maintains the distinction between an amyotrophic lateral sclerosis and a chronic poliomyelitis. He says, "The absence of any spastic symptoms and the loss of the tendon-reflexes favour the diagnosis of chronic poliomyelitis. If the reflexes are increased or a Babinski response is present, the case is probably one of amyotrophic lateral sclerosis." He insists that in chronic poliomyelitis the weakness of the muscles occurs before the wasting, whereas in amyotrophic lateral sclerosis the wasting is the primary symptom. In chronic poliomyelitis the legs and shoulder muscles are most often affected, whereas in amyotrophic lateral sclerosis the small muscles of the hand are more often involved. Whilst admitting the points above mentioned as variations in symptoms of the disease, we are not prepared to accept them as distinguishing features of such importance as to warrant the recognition of two distinct diseases.

**Pathology.**—The essential lesion in the group of cases dealt with in this article is a primary degeneration of the cells of the ventral horns of the spinal cord, usually associated with a similar degeneration of the homologous motor nuclei of the brain-stem, and a consecutive atrophy of the voluntary muscles innervated by the affected cells. In almost all cases there is also, as Sir W. Gowers first insisted, a primary degeneration of the pyramidal tracts or upper motor neurons. Experience has shewn that this may be often found in cases in which there were not any spastic symptoms during life, but it must be admitted that the upper motor neurons have been intact in a few cases examined by adequate methods (J. B. Chareot, Williamson, Cassirer and Mass). Such cases, however, are rare, and only form one end of a long series in which the relative amount of the affection of the upper and lower motor neurons varies very much. At the other end of the series are cases in which the ventral horns have been almost intact while the pyramidal tracts were intensely degenerated (Strümpell). Progressive muscular atrophy and amyotrophic lateral sclerosis have been frequently regarded as the prototype of the motor system-diseases; but, though their clinical features may justify this view, it will be shewn that anatomically the disease is rarely limited to the motor neurons.

The intensity of the disease of the grey matter of the spinal cord varies with the severity and the rate of evolution of the clinical symptoms, and is consequently usually most advanced in the lowest part of the cervical enlargement. Here all the larger cells of the ventral horns may have disappeared or shew severe regressive changes. They gradually shrink in size, lose their processes, and become oval or spherical in shape; their Nissl bodies gradually disappear, and the nuclei shrink and become

irregular and distorted. One of the most constant and prominent changes in the degenerating cells is a great increase of yellow intracellular pigment, which is usually laid down in a single mass near the nucleus or at a pole of the cell; as it increases it displaces the nucleus and the other functional elements of the cell, and finally many cells are represented only by a mass of pigment apparently contained within the cell-wall, with a distorted nucleus lying by its side. These degenerated structures disappear more slowly; in several cases we have seen them invaded by neurophages, and at a later stage only groups of such neurophages laden with nerve-cell pigment mark the position from which a cell has disappeared. The affection of the nerve-cells is thus a slow atrophic process; definite chromatolysis is very rare, and is usually found only in cases of acute course.

In sections stained with Weigert's method it may be seen that the reticulum of myelinated fibres has almost disappeared from the ventral horns, only the fibres or reflex collaterals that come from the dorsal roots remaining intact; Marchi's method may demonstrate the products of their degeneration, and especially the affection of the intra-medullary portions of the ventral roots. The degeneration of the cells and fibres of the ventral horns leads to a secondary proliferation of neuroglia in them, with increase of its nuclei and fibrillar elements, and frequently, most often in cases of rapid course, the blood-vessels are congested, and there may be a moderate small round-celled infiltration of their walls. Recent haemorrhages have been also observed, but there can be no doubt that these vascular changes are entirely secondary to the degeneration of the nervous elements; Haenel's suggestion that the vascular disturbances are primary and the nervous degeneration secondary thereto cannot be accepted. In the grey matter of the cord the disease is usually limited to the ventral horns; the dorsal and lateral horns are almost invariably intact, but degenerative changes have been occasionally found in Clarke's column associated with degeneration of the spino-cerebellar tracts.

The nuclei of the motor bulbar nerves are similarly affected in cases with bulbar symptoms. The hypoglossal and spinal accessory nuclei usually suffer the most severely, but the nucleus ambiguus, which is the only vagus nucleus that is involved, as it alone sends somato-motor fibres to the vago-glossopharyngeal roots, the facial, and the motor nucleus of the trigeminus, are similarly affected. The sensory cranial nerves invariably escape. The oculomotor nuclei are but rarely affected. Brasch, however, described degeneration in the posterior portion of the 3rd and 6th cranial nuclei. The disease of the grey matter is thus essentially a primary degeneration of the nervous elements with a resulting neuroglial sclerosis, and occasionally some vascular reaction. But those who separate a chronic anterior poliomyelitis from progressive muscular atrophy, a separation not accepted here as the pathological distinctions proposed are as vague and unsatisfactory as the clinical, assume that in this class the lesion is a subacute inflammation of the grey matter by which the nervous elements are destroyed. In very few of the cases





recorded under this title, however, is there convincing evidence that the primary disease was inflammatory, and in many there was also a pure system-degeneration of the cortico-spinal tracts.

The intra-medullary segments of the motor roots degenerate parallel with the ventral horn cells from which they take origin, but it is remarkable that though the degeneration of these cells may be extreme or even complete there may be very little change in the extra-medullary portions of the ventral roots or in the corresponding motor nerves, even though there is very intense degeneration of the muscles supplied by them. Attention has been repeatedly drawn to this (Kronthal, Hoche, Nonne), and it seems impossible to explain it merely by the rapid removal from the peripheral nerves of the degenerative products by which the Marchi method indicates the affection. Often, however, the affection of the motor nerves is parallel to that of the cells from which they take origin.

The affected muscles feel soft and flabby, and appear pale to the naked eye; or as the changes are rarely universal, the muscles may appear streaky, the diseased portions being indicated by their pallor. The predominant change visible under the microscope is an atrophy of the fibres to a calibre much less than the normal; their transverse striation generally remains distinct, but there is constantly a great numerical increase of their nuclei. When the degenerated fibres disappear completely, the positions they occupied may be marked only by clumps of these nuclei which persist in the connective tissue. More rarely fibres increase in calibre, and undergo regressive changes, such as fission and vacuolation. The disease of the muscles is characterised by its irregularity; bundles of normal fibres may be generally found interspersed among degenerated ones. As the regressive changes proceed in the muscles new fibrous tissue is laid down; there is never such an excess of fat as in the primary muscular dystrophies. The unstriated muscles escape, though in one case Léri observed atrophy of the muscular coats of the intestines and bladder.

The more exact the methods of examination, the more frequently has degeneration of the pyramidal tracts been found; as in many cases their degeneration is marked only towards the later stages of the disease, the employment of the Marchi method is essential, and it is the more so in cases of rapid course. In the cord, the direct and crossed pyramidal tracts are equally involved where the former exist, but the degeneration is partial as all the pyramidal fibres do not suffer. It can be usually followed up through the whole of the brain-stem, though in some cases in which the examination was apparently satisfactory, it ceased at the upper end of the cord or at some point in the brain-stem (Lejonne and Lhermitte, Puscariu and Lambrior). Kojewnikoff in 1883 first traced it still higher through the posterior limb of the internal capsule to the cortex of the Rolandic gyri, and since the Marchi method has been commonly employed, this observation has been repeatedly verified (Mott, Spiller, Probst); in a series of 10 successive cases the degeneration of the upper motor neurons in their whole course was demonstrated by this



method (Holmes). The fibre degeneration is found chiefly or solely in the anterior central gyrus, and corresponding thereto definite changes are usually present in the cortex of this region. These consist of a slow atrophy or degeneration, and eventually disappearance in the more chronic cases, of the large pyramidal cells (Betz-cells) that characterise the precentral cortex; this change is very similar to that which the ventral horn cells undergo. It is from these cells that the fibres of the pyramidal tracts take origin (Holmes and May). The existence of this cortical disease was first observed by Charcot and Marie, and it has been repeatedly confirmed (Campbell, Mott and Tredgold, Holmes).

It is usually evident that the degeneration of the upper motor neurons is oldest and most complete, that is, it involves a greater proportion of the fibres towards their termination in the spinal cord; this makes it probable that it commences in the portions of the fibres farthest from their cells or trophic centres, and that the fibres die back towards their cells in the cerebral cortex. But amyotrophic lateral sclerosis is distinguished from the other system-degenerations by the fact that these neurons are affected more as a whole; for in acute cases the Marchi method may shew a degeneration almost as intense in the cerebral cortex as in the spinal cord, and the affection of the Betz-cells is certainly not secondary to that of the fibres arising from them. But though the upper motor neurons die as a whole, the structural change may be earliest demonstrable in their most distal portions.

The degeneration of the white matter of the cord is not, however, confined to the pyramidal tracts; there is invariably a diffuse degeneration of the rest of the ventro-lateral columns, usually most marked in the shorter fibres that surround the ventral horns. These are the fibres that take origin from the smaller cells that lie in the more dorsal portions of the ventral horns and connect different segments of the cord with one another; the cells that give them origin have been found in the same state as the larger root-cells of the ventral horns (Ballet). The ventro-lateral columns have been found affected in cases in which the pyramidal tracts were intact (J. B. Charcot). Degenerated fibres are usually found in the ventral commissure too. In many cases there is also some degeneration of the spino-cerebellar tracts, especially of the direct cerebellar tract, which may be traced to the cerebellum (Pal, Miura, Philippe and Guillain, Sarbó, Holmes); degenerative changes have been also observed in Clarke's column, from which the direct cerebellar tract arises. Some authorities, as Oppenheim, would exclude the degeneration of the spino-cerebellar and other non-motor tracts from the disease; but it has been observed so frequently that this attitude cannot be maintained. The dorsal roots and the dorsal columns of the cord are usually intact, but a slight sclerosis of Goll's column is occasionally present; it is generally nothing more than may be frequently seen in old age, but a more acute degeneration has been described (Pal, Mott and Tredgold).

In the brain-stem the dorsal longitudinal bundles frequently contain degenerated fibres which diminish in number towards the brain, though some

can be traced to the upper part of the mid-brain; these degenerated fibres seem to come from the ventral columns of the spinal cord. Other fibres from the ventro-lateral columns terminate in the substantia reticularis of the lower half of the medulla dorsal to the inferior olives. The longer tracts of the brain-stem are usually unaffected, but the fillet occasionally contains degenerated fibres; many of these are generally pyramidal fibres which join the fillet in the mid-brain, to pass, presumably, to the nuclei of the motor cranial nerves. Probst has recorded degeneration of the tecto-spinal tracts and of von Monakow's bundle. The optic thalamus and corpus striatum are not involved, but the middle portion of the corpus callosum frequently contains degenerated fibres (Probst, Mott, Spiller, Rossi and Roussy); these degenerated callosal fibres are probably collaterals of the pyramidal tracts (Cajal).

The mutual relations of the degeneration of the upper and lower motor neurons have been much discussed. According to Charcot the disease first affects the lateral column, and later passes into the ventral horns; von Leyden, on the other hand, thought that the disease of the ventral horns is the primary change, and that it invades the upper motor neurons by passing over the motor inter-neuronic synapses in the ventral horns. But as on the one hand the ventral horn cells are rarely influenced by degeneration of the pyramidal tracts, and as on the other the pyramidal fibres do not degenerate secondarily to even intense ventral horn disease, as in infantile palsy, neither hypothesis can be seriously entertained. The degeneration of the upper and lower motor neurons is often simultaneous, or at least so independent that neither can be regarded as the cause or consequence of the other. This view can be readily accepted, as the disease is usually not limited to the purely motor tracts.

The cause of this primary degeneration of the affected neurons is obscure. Strümpell postulated an inherent tendency to degeneration, an abiotrophic constitution; but there are no data in favour of this hypothesis, except the very rare hereditary or familial tendency of the disease. There is as little to support the assumption of extrinsic factors, such as the action of toxins, though certain poisons, such as lead, are not without influence. It is difficult to see how injury, as Erb and others assume, can determine the widespread degeneration that is the basis of the disease; but the not infrequent occurrence of the disease in the later life of persons who had infantile paralysis in childhood indicates that local lesions may have some influence.

**Etiology.**—The cause of the disease is unknown. Prolonged hours of work and fatigue seem to be factors in determining the starting-point of the atrophy. Sometimes the atrophy is attributed to a blow. There is fairly good evidence that lead (Wilson) and syphilis (Lannois, Dana, Merle) may produce the condition. Other poisons, both organic or inorganic, endogenous or exogenous, probably act like lead, and start the degeneration.

The disease commonly affects those in the latter half of life, and men

more often than women. Progressive muscular atrophy occurs in children, and even in infants, but these cases for the most part correspond to a toxic degeneration of the lower motor neurons. In some of the recorded cases several members of the same family have been successively affected (Hoffmann, Werdnig, Senator, Beavor). These cases will be described on p. 714.

*Heredity.*—There is some evidence that this affection is rarely hereditary (Gowers, Bruining). Drs. Gee, Ormerod, and Holmes have published examples of progressive muscular atrophy of the hands occurring in several members of a family, rather closely resembling these cases.

*Symptomatology.*—For convenience, the disease will be described as it affects different parts of the nervous system: (1) Symptoms produced when the lower neurons of the upper extremities and neck are first affected; (2) Symptoms produced when the lower neurons of the bulb and oculomotor nuclei are first affected; (3) Symptoms produced when the lower neurons of the lower extremities are first affected; (4) Symptoms produced when the upper neurons are affected.

(1) *Symptoms produced when the Lower Neurons of the Upper Extremities and Neck are first affected.*—The first thing that a patient complains of is some weakness of certain muscles of the upper limb of one side; the muscles most frequently attacked are the small muscles of the thumb, and the first movements to be affected are the delicate and complicated movements of picking up a pin or fastening a button. Pain and all affections of sensation—such as tingling, numbness, and anaesthesia—are, as a rule, absent. The difficulty of performing certain movements directs the patient's attention to the thumb, and very soon he notices a distinct flattening of the thenar eminence.

On examination there is found some wasting of the small muscles of the thumb, with weakness and defect of two principal movements, namely, abduction of the thumb and opposition of the thumb: the former is best tested by laying the hand flat on the table with the palm upwards, and making the patient move the thumb upwards away from the palm. By opposition we mean the power of touching the tips of all the fingers in succession with the tip of the thumb, and more effort in opposition is required in the case of the index finger than of the fourth finger. As a rule it is not possible to detect the order in which the different small muscles are attacked, but the two movements mentioned above cannot be performed by the long flexors and extensors of the thumb in the absence of the small muscles. Again, flexion of the metacarpo-carpal joint cannot be performed by the long flexor alone, unaided by the small muscles, without antecedent flexion of the other joints of the thumb. The first interosseous muscle is usually next attacked; its weak action is shewn by an inability to abduct the first finger from the middle finger, and its wasting by the absence of the muscular swelling on the dorsal aspect when the patient presses the thumb firmly against the metacarpal bone of the index finger. Defects of the other interossei are shewn by the difficulty of separating or abducting, and adducting each finger when



the palm is placed flat on the table (as it is not possible to separate the fingers when they are flexed at the metacarpo-phalangeal joints), and by the hollowness of the interosseous spaces. Wasting of the hypothenar eminence and any inability to abduct the little finger indicate the extension of the disease to the small muscles of the little finger. One hand is usually affected before the other, and with about equal frequency on the two sides; but in a few months the other hand becomes involved in a similar manner. The disease is always bilateral, and generally symmetrical.

Before the small muscles of the hand are completely paralysed the flexors and extensors of the forearm usually become implicated; but if this be not the case, the hand assumes a peculiar clawed shape—the “*main en griffe*.” This state, which was first explained by Duchenne, is due to the loss of power of the interossei, whose action is to flex the metacarpo-phalangeal joints of the fingers and to extend the phalangeal joints; hence when the interossei are paralysed there is flexion of the phalangeal, and hyper-extension of the metacarpo-phalangeal joints of the fingers. In extreme cases the thumb becomes so rotated outward that the palmar surface of the thumb looks the same way as that of the fingers; and, owing to the atrophy of the lumbricales, the flexor tendons can be seen in the palm of the hand. Associated with atrophy and paralysis of the hand muscles, contraction of the pupil on the side most affected is sometimes observed, with loss of dilatation to shade; this is due to the implication of the dilator fibres of the iris which come off from the second dorsal root to join the sympathetic. After the muscles of the hand the muscles of the forearm are usually the next to be affected, and, as a rule, the flexors before the extensors, and the flexors of the fingers and thumb before the flexors of the wrist; on the other hand, the extensors of the fingers and thumb are usually affected before the extensors of the wrist.

In the upper part of the arm the muscle which is usually next to be affected is the deltoid, the rounded contour of the shoulder being lost and the head of the humerus being felt; after that follow the biceps, the brachialis anticus, and then the supinator longus; the supra- and infraspinati are usually affected at the same time as the deltoid, and the teres major and minor and subscapularis also become involved. The serratus magnus is often attacked, and if the deltoid be strong enough to advance the humerus to the horizontal line, the posterior border of the scapula projects like a wing, owing to paralysis of the serratus. The rhomboids and the middle and lower part of the trapezius are often wasted, but the highest part of the trapezius between the occipital bone and the clavicle always escapes. Three other muscles nearly always escape; namely, the triceps, latissimus dorsi, and the lower half of the pectoralis major. The upper (clavicular) half of the pectoralis major is usually involved along with the deltoid, and in this case the action of advancing the humerus to the horizontal line is lost; but the upper part of the pectoralis may still retain its power of acting with its lower (sternal) half in adducting



the humerus,—thereby giving an instance of paralysis of a muscle of a limb from a spinal cord lesion, for one form of movement but not for another.

The condition of most of the above muscles can be ascertained by their wasted condition and failure to move the joints; but there are two muscles between which it is often difficult to make a diagnosis, namely, the trapezius and serratus; for a projecting scapula, when the arms are advanced, may occur with paralysis of the middle part of the trapezius, or with that of the serratus. When the deformity is due to paralysis of the trapezius, no fibres can be brought out by direct faradisation over the paralysed part of the muscle, and the patient is still able to draw the scapula forward, as, for instance, in pushing with the extended arm; moreover, the posterior border of the scapula projects when the humerus reaches the horizontal line, owing to the scapula not being kept applied to the chest-wall by the trapezius, while above this line the deformity disappears as the lower end of the scapula is rotated forwards by the serratus; whereas in paralysis of the serratus magnus, the separate movements of elevation of the advanced humerus above the horizontal line, and of drawing forwards of the scapula, as in pushing, are not possible, and the faradic reaction of the serratus muscle may not be obtained. This last defect, however, is an uncertain symptom, as it is difficult, especially in stout people, to faradise the muscle even in health.

The muscles of the neck, especially the extensors, are liable to be affected; and in extreme cases the head falls forward like a dead weight, and can only be extended by the patient jerking his head backwards, so as to get the centre of gravity of the head behind the spine; the sternomastoids are not affected as a rule. Of the other trunk muscles those of respiration are the most important. The most common condition is a palsy of the intercostals, when the respiration is purely diaphragmatic, but in some cases the reverse is the case; the abdominal muscles, such as the rectus abdominis, are affected less frequently.

A progressive muscular atrophy may occur in a patient who has been the subject of an acute poliomyelitis, and this combination of disease has been noticed rather too frequently to be purely accidental. Out of 36 collected cases, Potts accepts 28 as genuine examples of progressive muscular atrophy following on acute poliomyelitis. In 18 of these the atrophy began in the limb previously affected. In Bernheim's patient infantile paralysis of the right leg appeared at the age of eleven months; when forty-four years old he had progressive muscular atrophy of the small muscles of the hand, and died four years later of cerebral haemorrhage. The cord showed characteristic atrophy of the cells of the anterior horns and sclerosis of the lateral columns. A similar case with a pathological examination is recorded by Cornil and Lépine.

*The electrical changes in the muscles* are of great importance, and are especially useful in distinguishing these cases from the myopathies. The most important changes found are in the muscles rather than the nerves. The nerves react normally to the faradic current, and also to the galvanic

current, so long as there are any fibres left to respond, but the amount of contraction produced is diminished; whereas the muscles which are wasted, while reacting through their nerves to the faradic current, shew the reaction of degeneration with the constant current by giving a slow contraction, and by reacting better to the anodal (positive) closure than to the kathodal (negative) closure. This is called *the partial reaction of degeneration*. In some cases, although the contraction be slow, the kathodal closure is equal to or even greater than the anodal closure; and the slow deliberate contraction of a muscle is more often an indication of degeneration than increased reaction to the anode. After a time the faradic reaction is lost in the nerve going to the muscle, and still later the reaction of the muscle itself to the constant current is not obtained.

Another symptom of much importance is *fibrillar contraction*. In a muscle which is beginning to suffer, a slight flicker may be noticed in the direction of the muscle-fibres. This is due to the contraction of individual fibrils, which start up under the skin, subsiding again immediately. The flickerings are increased by mechanical irritation, as by tapping the muscle, or when the muscles are fatigued. They do not occur in muscles too much wasted to have any fibres left to contract. They are probably due to a hyper-excitability of the degenerating cells in the anterior horns of the spinal cord. In some cases the fibrillar contractions are so strong as to flex or extend one finger involuntarily. Besides the fibrillation, *the reaction of the muscle to direct percussion* over its motor point is more readily obtained than in health.

(2) *Symptoms produced when the Lower Neurons of the Bulb and Oculomotor Nuclei are first affected*.—In bulbar paralysis the symptoms are bilateral, and, as a rule, come on gradually, with slight difficulty in speaking; but sometimes the difficulty is first noticed when the patient tries to sing, and after that the speech gradually becomes indistinct.

The tongue is usually the first organ to be attacked. This is shewn in the difficulty of pronouncing certain consonants which are produced by the action of the tongue as it is approximated either to the teeth—dental consonants—or to the soft palate—guttural consonants. In the former case *t*, *d*, and *th* are difficult to pronounce and are first affected, and subsequently the consonants *k*, *g*, and *ch*. General weakness of both sides of the tongue is observed, with wasting of its muscular tissue. At first the tongue looks flatter and not quite so plump as in health, the movements become slower, and there is difficulty in protruding the tongue to the full extent beyond the teeth, and also in putting the tip into either cheek, or in elevating it. Early in the disease fibrillar contractions are observed in the form of fine linear quiverings taking place along the tongue in a longitudinal direction under the mucous membrane.

After the tongue the orbicularis oris is next involved, and the patient cannot purse up the mouth, and loses the power of whistling (in trying this test the anterior nares should first be closed, as the soft palate is often unable to close the posterior nares), or of blowing out a candle. In the

early stages the strength of the orbicularis oris may be tested by inserting the forefinger and thumb between the lips, and by trying to separate the finger and thumb against the pursed-up lips; in a healthy person this is not easy. At the same time the speech is still further affected, and especially the explosive labial sounds *p*, *b*, although the aspirate labial sound *f* and the resonant labial *m* can still be sounded, as in these two sounds the lips are not required to be tightly closed. As the paralysis progresses the transverse length of the lips is increased, and the muscles of the chin are involved.

The occurrence of progressive ophthalmoplegia is associated with a bulbar paralysis, and in rare instances with progressive muscular atrophy. There is not, however, much pathological evidence; Guinon and Parmentier have recorded and collected cases which must be accepted, and Brasch has recorded a case with a careful pathological examination. Wilbrand and Saenger have analysed the cases. The Argyll Robertson pupil has been noted in association with progressive muscular atrophy. Although its presence must always raise the possibility that syphilis is responsible for the disease, recorded cases seem to shew that this pupil reaction has been present when syphilis could be excluded (Wilson).

The other muscles of the face, including the zygomatici and the elevator of the upper lip as well as the orbicularis palpebrarum and frontalis, are not affected as a rule. Hence the naso-labial fold is often well marked, and this, coupled with the transverse line of the lips, gives the patient a curious lugubrious expression which is very characteristic.

Paralysis of the soft palate on both sides gradually ensues, the effect of which is to alter the speech very characteristically; and it is important to note that a slight weakness in elevation of both sides will produce much more effect on the voice and on the power of closing the posterior nares than an almost complete paralysis of one-half only. In a paralysis of both sides of the palate, which is sufficient to prevent the patient from closing the posterior nares, the speech is nasal, the difficulty of pronouncing the gutturals *k*, *g* by pressing the tongue against the soft palate is increased; also, as some of the air passes through the nose, the proper amount of pressure to separate the lips is not obtained, so that *p* and *b* become *v* or *f* and *m*. On trying to inflate the cheeks—taking care that the lips are closed voluntarily or by the finger and thumb—a snorting noise is heard as the air passes through the posterior nares; or, if the anterior nares be closed by the finger and thumb and the cheeks inflated, then, on releasing the anterior nares, the air rushes through and the cheeks collapse. On phonation, and on a deep inspiration, the soft palate on both sides is very slightly elevated; but the mere hanging of the uvula to one side, or the difference of the height of the two palatine arches, is not of much value, and paralysis of the soft palate can only be said definitely to occur when there is deficient movement on phonation or respiration.

The vocal cords are also liable to be paralysed after the above parts have been involved; and the palsy consists in a difficulty in approximating



the cords in phonation and in coughing, so that the voice is low-pitched and monotonous, and a proper cough cannot be executed.

In some cases the muscles of mastication—the masseters, temporals, and pterygoids—become involved, and then the patient has difficulty in making the teeth meet, and in masticating the food; and the mouth remains open.

The paralysis and the wasting of the muscles progress till the patient's condition becomes most deplorable. The features present the characteristic melancholic appearance, the mouth cannot be closed, the lower lip is everted, the tongue lies shrivelled up without any power to move off the floor of the mouth, the soft palate hangs motionless, or flaps to and fro with respiration. The speech is a slow monotonous mumbling or is lost altogether, or the power of phonating a few vowels is all that remains. Mastication is almost impossible, owing in part to the feebleness of the muscles, and in part to the inability of the tongue to keep the food between the teeth.

The act of swallowing is attended by the greatest difficulty and danger. Owing to the paralysis of the tongue the food cannot be pushed backwards by the pressure of this organ from before backwards against the hard palate, but the head has to be thrown backwards to allow the food or liquid to fall backwards by its weight; fluids when they reach the back of the mouth, as the posterior nares are not shut off by the soft palate, readily pass into the nasal cavity and regurgitate through the anterior nares. Again, as the larynx is not drawn up under the tongue, and as the epiglottic muscles and the constrictors of the pharynx are palsied, fluids very easily pass into the glottis instead of into the oesophagus, and frequently produce choking, whilst the power of expulsion is scarcely assisted by the feeble power of coughing possessed by the patient. Later in the disease the vagus nucleus is sometimes invaded, giving rise to rapid cardiac action and to attacks of dyspnoea.

Owing to the difficulty of swallowing, the saliva accumulates to an extraordinary amount; and, owing to the drooping of the lower lip, the saliva is constantly dripping from the mouth, and the patient saturates many handkerchiefs in the day; on opening the mouth the saliva, which is often thick and viscid, hangs in festoons about the fauces, and every now and again the patient throws back his head in the endeavour to get rid of the excess of saliva by swallowing.

The wasting of the muscles is very well marked and does not follow the loss of power, as in acute nuclear lesions, but goes on step by step with the weakness; it is very gradual and involves fibril after fibril in the tongue. The atrophy of the intrinsic muscles of the tongue can be felt with the finger and thumb, and the mucous membrane is thrown into folds. The lips are sometimes not noticeably diminished in size, in others they are decidedly thinner than normal. Wasting of the levator palati and of the vocal cord muscles cannot actually be seen, but their loss of action can be readily ascertained.

The fibrillar contractions are similar to those seen in the atrophic



museles of the arm; they are best seen in the muscles which are wasting, and especially in the tongue, which looks like a bag half full of worms. The individual fibrils contract one at a time and in succession; movements which are probably due to irritation of the hyper-excitabile degenerating nerve-cell in the nucleus supplying the individual fibril.

With regard to the electrical reactions, the affected museles react to the faradic current as long as there are any musele-fibres left, which have not degenerated so far as to fail to respond to the current; but as these fibres diminish in numbers with the progress of the disease, so the force of the resultant contraction becomes less and less. But these degenerated musele-fibres which will not react to the faradic current will give the reaction of degeneration with the galvanic constant current; thus, we have the musele giving a slow deliberate contraction with a weaker galvanic current than natural, and responding, on making the current, more readily to the positive than the negative pole. We have, therefore, the following conditions: in the earliest stages the muscles react to both currents, though not so strongly as normally; later, when about half the fibres have degenerated, the faradic reaction is about half as strong as it should be, whilst to a fairly strong constant current the quick normal response of the healthy muscle-fibres to the negative closure is followed by a slow deliberate contraction of the degenerate muscles; if the minimal current only is tried, the slow reaction of the degenerate muscles will be obtained, and probably with the positive rather than with the negative pole. Finally, when all the fibres have wasted there is no reaction to either current.

Reflex action of the larynx and pharynx is almost invariably diminished and after a time abolished; so that on touching the soft palate it is either only slightly elevated or not at all; whilst by tickling the fauces there is great difficulty in producing the reflex action of retching and vomiting.

(3) *Symptoms produced when the Lower Neurons of the Lower Extremities are first affected.*—It is much rarer for the wasting and loss of power to begin in the muscles of the lower extremity than in the upper. When this does occur, the anterior tibial muscles are those most commonly affected, but the atrophy may extend to the muscles of the thigh and the flexors of the hip. Fibrillar tremors are seen in the museles, and electrical examination of the muscles shews the same partial reaction of degeneration as is seen with the affection of other parts. In whatever portion of the body the disease begins, it tends to pass into other regions. When the disease starts in the bulb, the progress may be so rapid that a fatal result occurs before any atrophy is noticed in the extremities; on the other hand, when the disease starts in the extremities, it is the affections of the bulb that commonly lead to a fatal result.

(4) *Symptoms produced when the Upper Neurons are affected.*—The symptoms produced by affections of the upper motor neurons are weakness and rigidity. The weakness and rigidity may affect any portion of the body, giving rise to the same symptoms as those produced by affections

of the lower motor neurons, but without the wasting and loss of tone in the muscles. The common type of the disease is that with weakness and rigidity of the lower limbs and muscular wasting in the upper extremity. The muscles of the lower extremity, although weak, are still developed and rigid; the knee- and ankle-jerks are increased, ankle-clonus may be present, and the plantar response is extensor. In the arms there is wasting of the small muscles of the hand, with weakness and loss of tone. In cases with wasting of the arm muscles the arm-jerks are often exaggerated, pointing to an affection of the upper motor neuron. It is only when the atrophy in the arms becomes advanced that the arm-jerks disappear.

The clinical features of Charcot's amyotrophic lateral sclerosis are a spastic condition of the legs combined with atrophy of the hand and arm muscles. Other evidences of affection of the upper motor neurons will be found in the increase of the jaw-jerk and the presence of jaw-clonus in certain cases. It is possible that in some cases the upper motor neuron may be affected without there being any evidence of implication of the lower motor neurons, but such cases are rare.

Cases occur in which there is no clinical evidence of affection of the upper motor neuron, whilst the lower motor neurons are markedly affected. In such cases marked degeneration of the upper neuron is not infrequently found on pathological examination.

**Diagnosis.**—In order to distinguish this form of progressive muscular atrophy from several other muscular atrophies, the following points should be borne in mind: in this condition the onset of atrophy is very gradual, and wasting does not follow loss of power, but accompanies it; fibrillar twitchings are present, and there is no alteration of sensation in any form.

*Differential diagnosis* must be made from the various types of myopathy, peripheral neuritis, toxic degeneration of the lower neurons, lesions of the spinal roots, pachymeningitis, pressure on the cord by growths, gumma, or tuberculous lesions, acute poliomyelitis, syringomyelia, haematomyelia, and disseminated sclerosis, and the atrophy which occurs from the presence of a cervical rib. Increase of the deep reflexes with signs of pyramidal involvement will help to separate the disease from the myopathies, peripheral neuritis, and lesions of the spinal roots.

A lesion such as a new growth, gumma, or tuberculous mass may press upon the cord, and give rise to the wasting of the hands and a spastic condition of the legs, but such a condition is usually attended with pain, and with alteration of sensation below the level of the lesion. In syringomyelia there are peculiar sensory changes in the limbs and trunk, tactile sensibility being preserved, whilst impressions of pain and temperature are lost, and frequently there are changes in the joints and skin. In disseminated sclerosis the muscles of the hands do not, as a rule, atrophy, and there are other symptoms, such as inco-ordination, nystagmus, and loss of sensation, which usually render the diagnosis easy; but in some cases, and especially those in which a spastic condition of the

lower limbs is the first symptom, diagnosis may be difficult or even impossible.

**Treatment.**—The general health of the patient should be maintained by fresh air, either in the country or the seaside; and, if the patient is fit for it, a sea-voyage should be recommended. Exercise should be taken in moderation, but should always fall short of tiring the patient. The removal of any toxic factor, such as lead and alcohol, is of the greatest importance. The teeth need careful inspection. When the muscles of the tongue and deglutition are affected the patient should be carefully watched during meals; in severe cases feeding by the nasal tube should be employed.

Local treatment has not much effect on the wasted muscles. Electrical treatment has been used very largely, and though the results are of doubtful value, it is at any rate a means of exercising the muscles without tiring the patient. It is best to employ the constant current with the positive pole to the back of the neck, and the negative gently brushed over the affected muscles, being careful to use the weakest current which will cause a contraction.

Massage and rubbing have been frequently employed; this treatment is found to be useful, yet it often fails to arrest the wasting. With regard to internal remedies, cod-liver oil, quinine, and the syrup of iodide or phosphate of iron are requisite to keep up the general health. Of special nerve tonics arsenic and strychnine are useful. According to Sir W. Gowers, strychnine is most effective when given hypodermically, and succeeds thus after it has failed when given by the mouth. He recommends the nitrate of strychnine given once a day, beginning with gr.  $\frac{1}{100}$  and rapidly going up to gr.  $\frac{1}{40}$ ; when the malady is apparently arrested the injections are intermitted for one week in every three or four. It does not seem to make much difference whether the injection be given in the neighbourhood of the affected muscles or elsewhere.

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THE PROGRESSIVE MUSCULAR ATROPHY OF INFANTS. — Closely allied to the above-described disease of the adult is a rare disease in infants and young children, first described by Werdnig and Hoffmann.

**Etiology.**—The cause of the disease is unknown, but in many instances several members of a family, all about the same age, have been affected (Werdnig, Hoffmann, Beever).

**Morbid Anatomy.**—The changes in the nervous system, which somewhat resemble those in the progressive muscular atrophy of the adult, are atrophy of the cells of the anterior horns, degeneration of the spinal roots, and atrophy of the muscle-fibres. Changes in the crossed pyramidal tracts are very slight, or altogether absent. In Beever's case there was some degeneration of the fibres in the posterior columns.

**Symptomatology.**—An apparently healthy and intelligent child, who



has made the normal progress of an infant for the first few weeks or months of life, begins, without sudden onset and without obvious cause, to lose power. The weakness is first noticed in the legs and in the hips; as the disease progresses the lower portion of the back becomes affected, so that the child is no longer able to sit up. The disease pursues a progressive course, the shoulders, thighs, upper arms, forearms, and legs being successively involved, and finally the muscles of the hands and feet. Fibrillar twitching of the muscles may be present, bulbar symptoms may supervene, and contraction of the limbs may be present in some cases. The limbs are usually absolutely flaccid, and the deep reflexes abolished. There is no pain or tenderness, and no disturbance of sensation.

The disease runs a slowly progressive course, death taking place from failure of respiration or from bronchopneumonia.

**Diagnosis.**—Although pathologically these cases closely resemble the progressive muscular atrophy of the adult, clinically they present considerable differences. The disease starts in the proximal muscles, and only later affects the muscles of the hand. The atrophy is not so striking as in the adult cases; in fact the infant often appears well-nourished. Cases with a spastic condition of the legs are rare.

The weakness which accompanies *rickets* can be recognised by the absence of atrophy and the presence of the deep reflexes.

From the myopathies it is extremely difficult to distinguish this disease, for the symptoms may be strikingly alike, the atrophy of the muscles may be similar, and the deep reflexes may be lost in both diseases. This difficulty is strikingly shewn in a case of myopathy recorded by Finkelburg. The presence of an extensor plantar response in an infant cannot be regarded as of diagnostic value. The familial nature of the disease is also common to both myopathic and myelopathic affections.

**Prognosis.**—The disease is progressive; in some cases its course is rapid, in others the disease lasts for several years.

**Treatment.**—No form of treatment has been found to be of any avail. Massage and passive movements may be used, and will serve to prevent contraction.

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From a clinical point of view it is better to describe all the acute bulbar palsies together, and to include in this group the lesions just above the nuclei, those affecting the nuclei themselves, and those just below the nuclei inside the medulla.

The acute palsies may be subdivided into (A) those which are sudden, and (B) those which are rapid in their onset.

**A. Sudden bulbar paralysis**, also called apoplecticiform.—The cause of these cases is always vascular; they may be due to a small haemorrhage, but much oftener to thrombosis or embolism of one or more of the branches which come off from the basilar or vertebral arteries.

The occlusion in most cases is due to thrombosis occurring in syphilitic or atheromatous arteries. In rare cases embolism of the basilar may ensue from endocarditis, but the result of this would produce symptoms much more extensive than paralysis of the muscles supplied by the bulbar nuclei.

The affection usually occurs in middle or old age, but cases due to embolism or to syphilitic arteritis may be met with in younger people.

*Symptoms.*—The most important point of distinction between these cases and those caused by other lesions of the bulb is the mode of onset: this is quite sudden, with vomiting or giddiness, and with or without loss of consciousness; or the patient goes to bed apparently perfectly well and wakes up in the morning with bulbar symptoms.

In an extreme case there is paralysis of both sides of the tongue, of the soft palate, of the power of swallowing, and sometimes of the vocal cords. In other cases the symptoms are not so extensive, and may affect one side only.

A man aged forty-two, who went to bed quite well, found on awaking in the morning that he could not swallow, and fluids were coughed out of the larynx or returned through the nose; besides this there was paralysis of the levator palati on the right side, so that on phonation the palate was drawn to the left; the tongue was not affected, except that on protrusion it deviated slightly to the left, and the vocal cords acted normally. There was no anaesthesia, and the reflex action of the soft palate on the two sides, though deficient, was equal. In this case the sudden onset in the night was caused by a vascular lesion, probably thrombosis; but the exact position of the lesion was rather difficult to decide. It was observed that in the act of swallowing the larynx was raised up, and therefore that inability to swallow was due to failure of the constrictors of the pharynx; and, as it is very improbable that paralysis of one side of the pharynx would prevent swallowing, it is more likely that both sides were affected. We have, then, to find some part of the nervous system, a lesion of which would cause paralysis of the right levator palati and both sides of the pharynx. The sudden onset in one attack was against the pseudo-bulbar form; for although the act of swallowing is certainly represented in the cortex cerebri at the lower end of the ascending frontal convolution, it is bilaterally represented, so that

it would be necessary to have a lesion in the cortex of both sides, or in both internal capsules, to abolish the power of swallowing; besides, the action of the various muscles taking part in swallowing are co-ordinated in the cortex, and on stimulation of it swallowing occurs as one act, whereas in this case part only of the movement was deficient. It is not known if the fibres from the pyramidal tract cross over to the "centre for swallowing" in the medulla as one bundle, but it is more probable that the fibres cross over separately to the different nuclei taking part in the action of swallowing. It would therefore seem possible in this case that these fibres from the pyramidal tract to the nuclei of the accessory nerve or of the glossopharyngeal nerve were affected just above the nuclei. In another case there was a sudden onset with giddiness but without unconsciousness, followed by paralysis of the soft palate and of the vocal cord on the same side, and loss of sensibility to heat and cold and to pain on the opposite half of the trunk and limbs, but not of the face. This was probably due to slight thrombosis affecting the accessory nerve of one side on its way through the medulla, or its nucleus, and the sensory tract for the conduction of temperature and painful impressions for the opposite limbs and trunk, in the lemniscus above the decussation of its fibres. In another case, a woman, aged thirty, suddenly had some loss of power and sensation on the left side of the body, and thickness of speech; on examination a few days later the power had been recovered in her limbs, but she was suffering from "crossed anaesthesia." Over the left half of the trunk and the left arm and leg there was some tactile anaesthesia, which was not complete, with some loss of sensibility to pain and temperature; this area extended up the neck and up the posterior part of the left side of the head to the vertex, but it did not affect the left face. On the right side of the face there was marked deficiency to tactile sensations over the area of the 5th nerve corresponding to the first and second divisions, and to a less degree of the third division. There was slight conjugate nystagmus in all directions. A few days later she had weakness of the right temporal and masseter muscles supplied by the motor part of the 5th nerve, and also of the right facial muscles. She also had attacks of vomiting and giddiness, with apparent revolution of objects from right to left. As the patient recovered from the symptoms, the seat of the lesion is a matter of conjecture, but it seems almost certain that it affected the nucleus or the fibres of the right 5th nerve on their way through the pons, thereby causing the anaesthesia of the right face and paralysis of the right muscles of mastication; and it also affected the lemniscus—the sensory tract—on the right side above its decussation, so as to involve the sensory fibres of the left half of the trunk and left limbs, while the sensory fibres to the left face escaped, their crossing being above the lesion. The affection of the right facial muscles was slight, and was perhaps due to extension of the disease to the fibres on their way to the facial nucleus from the opposite pyramidal tract. As she had weak cardiac action, the case was probably one of thrombosis of the branches



of the basilar artery to the pons. Recently Dr. S. A. K. Wilson, from a critical analysis of the symptoms of these cases, has shewn that they are due to thrombosis of the posterior inferior cerebellar artery, the characteristic features of such a lesion being hemiataxia, unilateral disturbance in the distribution of the 8th, 9th, and 10th cranial nerves, disturbance of the cervical sympathetic on the same side, and a crossed dissociated anaesthesia.

In a case described by Senator a man, aged seventy-one, had a sudden attack of giddiness, vomiting, trouble in swallowing, and numbness in the left half of his face and left arms, and in both arms; the lower part of the left face was paretic, the tongue was protruded to the left, the legs were weak, the knee-jerks were absent, and there was deafness on the left side. After death a softened patch was found on the floor of the left half of the 4th ventricle 7-8 mm. long by 4 mm. broad, and extending between the olive and the corpus restiforme. Van Oordt published a case of sudden onset in which the symptoms were inability to swallow, nasal speech, paralysis of the right half of the tongue, and of all the muscles supplied by the right facial nerve, including the orbicularis palpebrarum, and right hemianaesthesia. On examination there was found, with arterial sclerosis, a softening patch on the left side of the medulla at the level of the middle third of the inferior olive, and affecting the formatio reticularis.

The symptoms differ as the lesion is above the nuclei, in the nuclei, or involves the nerves coming off from the nuclei on their way through the medulla. Besides the grouping of the muscles affected, the condition of the nutrition of the muscles and their behaviour to electrical testing and to reflex irritation are very important.

The acute and sudden bulbar lesions which involve the nuclei, and the nerves which come off from them, differ in their symptoms from lesions above the nuclei in the distribution to the muscles, and in causing wasting of the muscles in addition to paralysis of their movements. It is difficult to make this out with regard to the soft palate and laryngeal muscles; but with the tongue, owing to the facility with which the tongue can be felt and seen, it is fairly easy to tell if the mucous membrane is thrown into folds owing to the wasting of the muscular tissue. The muscles would also lose their reaction to faradisation, and would give the slow deliberate reaction to the constant current, reacting to the positive closure sooner than the negative—so that ACC is greater than KCC. The electrical reactions of the tongue and the levator palati can readily be ascertained.

The reflex response of the soft palate to irritation of the fauces is also lost or very much diminished when the lesion is in the accessory nucleus or the nerve coming from it, so that if one nucleus is affected the palate is drawn up reflexly towards the non-paralysed side only, and not raised at all if both nuclei are involved.

The wasting of the muscles and the loss of reflex action are due either to the isolation of the muscles from their trophic centre in the

nuclei, or to destruction of this centre; it is often difficult, therefore, if not impossible, to discriminate between the lesion of the nucleus and of the nerve coming from it. In the case of the hypoglossal nerve, however, owing to the proximity of the nerve to the pyramidal tract, there is more probability of some paralysis of the opposite limbs than if the lesion be in the nucleus; whilst the orbicularis oris is liable to be paralysed when the nucleus is affected, and not the nerve only. The distribution of the muscles affected is that pertaining to the particular nucleus or nerve involved; but the muscles supplied by a bulbar nucleus do not always correspond to those by its nerve, as the latter may receive fibres from other nuclei before it leaves the medulla.

If there be no wasting of the muscles, and no electrical changes, and if reflex action be preserved, the lesion must be above the nuclei; but it is often very difficult to tell whether the lesion be in the bulb just above the nuclei, or higher up in the motor path. The mode of grouping of the muscles affected by supra-nuclear lesions is different from that of nuclear lesions, for as the cortex cerebri knows nothing of individual muscles, but is concerned with movements only (Hughlings Jackson), the paralysis which occurs from lesions of the cortex or pyramidal tracts of both sides will be that of complete co-ordinated movements; for instance, in lesions of both pyramidal tracts one would expect that all the muscles entering into the complex movement of the first stage of swallowing would be paralysed, whereas in a nuclear lesion it would be possible for some of the muscles to be paralysed and not others, the paralysis in one case having a physiological grouping, in the other an anatomical.

Of the difference of the grouping of the muscles affected in double cortical or pyramidal lesions, and in a single lesion involving the pyramidal fibres as they are decussating at the middle line to reach their nuclei, it is difficult to speak definitely, and theoretically the grouping of the latter should be physiological; but in the case already mentioned some only of the muscles of swallowing were affected; and this was also found in a case published by v. Leyden. With regard to double lesions, complete paralysis of the movements of mastication and of swallowing, of the vocal cords and of the tongue, cannot follow a lesion of the cortex or the motor tract, unless it be bilateral, for in the above movements the muscles of both sides are represented in each hemisphere; thus, if one hemisphere is paralysed, the opposite hemisphere can carry on the work, but if both are affected, all voluntary movements are lost and reflex action only is retained. Hence in these cases there is a history of two or more attacks.

Cases of double hemiplegia producing these *pseudo-bulbar symptoms* have been described by Lépine, Jolly, Eisenlohr, Kirchhoff, Ross, Barlow; one of the most important being Sir T. Barlow's, in which there was found on necropsy softening of the 2nd and 3rd frontal and ascending frontal convulsions of both sides, producing in the first attack right hemiplegia, followed in four months by a second attack of left hemiplegia, with symptoms of inability to shew the teeth, to protrude the tongue, or

to talk, though he could understand signs; swallowing was difficult, and there was weakness of the limbs. In the case of a woman in whom the two attacks were separated by an interval of four months, the first attack gave rise to thickness of speech, and weakness of the left side; in the second attack she lost all power of speaking and even of phonation, was unable to swallow, and the right arm was weak; two years after the first attack there was still complete paralysis of the soft palate on both sides to voluntary efforts, with preservation of reflex action and electrical reactions. In this case the lesions were probably thrombotic and affected the anterior limb of the internal capsule of one side and, later, that of the opposite side. Other cases have been described in which vascular lesions have been discovered in the internal capsule and lenticular nucleus of both sides; as in one described by Dr. Newton Pitt, in which the paralysis of the face and tongue, and of swallowing, was very complete. In another case, published by Drs. Hughlings Jackson and Taylor, the patient had two attacks of hemiplegia affecting opposite sides, several years elapsing between the two attacks. The onset in the first attack was sudden, and articulation was lost for a week; in the second the left side was affected with a sudden onset, the patient could not protrude the tongue, and swallowing and speech were very difficult. The whole left side of the face was weak, the soft palate was completely paralysed, and the limbs of both sides were weak. Both pyramidal tracts were degenerated and sclerosed.

The mode of onset in all these cases by two attacks, affecting first one side and then the other, and the affection of the limbs are symptoms of lesions seated in both motor paths rather than of a single lesion at the point of decussation of the fibres from the motor paths just above the nuclei (*vide* also Vol. VIII. p. 106).

**B. Bulbar Paralysis of Rapid Onset.**—This second form, also included under the term “acute,” has a rapid onset, but takes some hours or a few days to develop. The nature of the lesion is the same as that of acute poliomyelitis, and cases will be found described under that title and also that of “polioencephalitis” (Vol. VIII.). The condition is not at all common, and the changes depend on an inflammation involving the nuclei of the bulb.

The *morbid changes* are similar to those of acute poliomyelitis, and consist of dilated vessels with exudation of leucocytes, and destruction of the cells of the cranial nuclei; or, in less severe cases, the nerve-cells lose their processes and shrink.

*Symptoms.*—In one case, described by Etter, the attack began, in a boy aged fifteen, with general malaise, headache and vomiting, pyrexia, and difficulty in swallowing; followed in the course of a week by paralysis of both sides of the face, the soft palate, the tongue on both sides, but especially the left, and the left 6th nerve. After death from pneumonia, acute myelitis was found on both sides of the medulla in patches involving the left 6th nucleus, the left facial nerve within the medulla, the left hypoglossal nucleus, the right facial nucleus, the right hypoglossal



fibres, the accessory nucleus of both sides, and below them the spinal cord as far down as the 4th cervical nerve.

Another case, described by Dr. W. Pasteur, occurred in a boy 2½ years old with a rapid onset of fever, diarrhoea, and sickness; the right facial muscles were completely paralysed with wasting, and there was difficulty of swallowing and paralysis with wasting of the right side of the tongue. Vandervelde has published a case of an acute inflammatory attack with fever and headache, causing paralysis of the middle and lower parts of the face, difficulty of swallowing, noises in the ears, and an inclination to fall to the right; at the necropsy leucocytes were found round the vessels and swollen axis-cylinders on both sides of the medulla.

**Chronic Bulbar Paralysis or Chronic Nuclear Paralysis.**—This condition is pathologically identical with progressive muscular atrophy taking place in other parts of the body and is frequently associated with it. It is therefore described with that disease under the heading "Motor Neuron Disease" (p. 708).

**Infra-Nuclear Paralysis.**—The symptoms of these lesions differ according as the position of the lesion is within the medulla itself, or outside the medulla pressing on this structure, or implicating its nerves before they emerge from the cranial cavity. The symptoms will have to be carefully distinguished from those produced by lesions of the bulbar nerves after they have left the cranial cavity, which hardly come under the title of bulbar paralysis.

*The infra-nuclear lesions within the medulla* must of necessity be very limited in range, as they take effect on the bulbar nerves only in their passage between their nuclei at the posterior part of the medulla and their exit from the surface of the medulla. The acute form has already been referred to (p. 721), and the most likely lesion would be softening caused by thrombosis of one of the vessels entering the medulla from the vertebral artery, and the symptoms would be sudden paralysis of the tongue muscles of one side, or of the soft palate and vocal cord of one side, with loss of power and perhaps anaesthesia of the opposite limbs and half of the body with escape of the face, while the trapezius and sterno-mastoid muscles supplied by the spinal accessory would not be affected. The half of the tongue and the soft palate would waste, and give the reaction of degeneration to electrical testing. A tumour within the medulla at this part would also give the same symptoms with a gradual onset, but the condition is very rare.

The *extra-medullary lesions* are more common and definite than the intra-medullary.

The symptoms may be due to a tumour pressing on the nerves and on the medulla, or to meningitis, which may be simple or syphilitic. Of these, gumma and syphilitic chronic meningitis are the most common. In syphilitic meningitis the membranes are very much thickened and compress the nerves passing through them, a condition which may be associated with a gumma in the neighbourhood or be independent of it.

The symptoms consist in a gradual paralysis of half the tongue, half



the soft palate, and one vocal cord, all on the same side. This combination, in cases of lesion outside the medulla, first pointed out by Dr. Hughlings Jackson in 1864, is due to the implication of part of the spinal accessory and the hypoglossal nerves. In some cases the other part of the spinal accessory is also affected, whereby the sterno-mastoid and trapezius of the same side are paralysed. The affected muscles waste, and, being cut off from their trophic centres, the bulbar nuclei, give the electrical reaction of degeneration. The symptoms do not cause the difficulty of the other forms of bulbar paralyses, as they are unilateral and the patient is able to speak, swallow, and cough by means of the unaffected opposite side.

**Extra-Cranial Causes.**—Although they are not included under the name "bulbar paralyses," we must remember that lesions of the lower cranial nerves outside the cranium give rise to symptoms which are often very difficult to diagnose from those of intracranial bulbar lesions. These lesions may be enumerated as caries of the cervical vertebrae, cellulitis of the neck, tumours, and multiple neuritis.

As an example of extracranial tumour, mention may be made of a case of complete paralysis of both sides of the soft palate in which reflex action and faradic excitability were lost, but the galvanic reaction of degeneration was present. The patient had not any paralysis of the tongue nor of the vocal cords, but the whole of the right 5th nerve, motor and sensory, was involved, with complete loss of taste for that side of the tongue. At the necropsy a sarcomatous tumour was found on each side at the back of the pharynx, but not extending across the middle line; and it had also spread backwards into the cranial cavity through the foramen lacerum medium on the right side, and attacked the 5th nerve near its root. The paralysis of the soft palate was considered during life to be due to inclusion of the pharyngeal plexus in the growth, whilst the freedom of the tongue and vocal cords was against the disease being intracranial, so far as the bulb was concerned.

Neuritis may affect single nerves like the hypoglossal, and hemiatrophy of the tongue in diabetes has been observed.

Very rarely cases of multiple neuritis occur in this region. Symptoms of bulbar paralysis commonly occur in myasthenia gravis, in diphtheritic paralysis, and more rarely in syringomyelia.

The general diagnosis of bulbar paralysis is of the greatest importance, and often also one of great difficulty.

The first point is to discriminate between the supra-nuclear lesions on the one hand and the nuclear and infra-nuclear on the other. In the supra-nuclear lesions the muscles do not waste, except from disuse, there are no fibrillar contractions, the electrical reactions are normal, reflex actions are preserved, and in some cases the emotional movements of expression; so that although the patient's face may be absolutely motionless to volitional efforts and he cannot cough voluntarily, he can cough, smile, and yawn reflexly, and the reflex actions of the soft palate and pharynx are also preserved.

On the other hand, in all nuclear and infra-nuclear lesions affecting the bulbar nerves, the muscles waste and give the electrical reactions of degeneration, and they sometimes present fibrillar contractions, and all reflex actions are either diminished or abolished altogether.

In supra-nuclear paralysees the pseudo-bulbar paralysees, due to lesions of the cortex or internal capsule, are characterised by a history of two attacks of hemiplegia involving the face, tongue, perhaps the limbs, first on one side and then on the other, and the symptoms occur after the second attack; whereas in lesions just above the nuclei the symptoms may come on after one attack, and the limbs may not be affected.

In the nuclear and infra-nuclear cases the first distinction is into acute and chronic cases. Taking the acute cases first, we have to separate them into those of sudden and those of rapid onset, the former being due to occlusion of a vessel or to a small haemorrhage, whilst the latter, being due to an inflammatory condition of the nuclear cells, would be attended by fever and vomiting. The diagnosis of acute nuclear from acute infra-nuclear lesions within the medulla would depend on the distribution of the symptoms. In nuclear paralysees it would be very difficult (except in the inflammatory form) for one hypoglossal nucleus to be affected without the other, and, furthermore, the orbicularis oris would probably be affected while the limbs would escape; whereas a lesion of the hypoglossal nerve in its intra-medullary course would not affect the orbicularis oris, and probably would cause weakness or anaesthesia of the opposite limbs.

The extra-medullary lesions are usually chronic with a gradual onset, and are nearly always unilateral; whilst the association of paralysis of the sterno-mastoid, trapezius, and also of the depressors of the hyoid bone, on the same side as the paralysis of half the tongue, the soft palate, and one vocal cord, would make the extra-medullary position of the lesion almost certain.

The prognosis with regard to life and recovery in the acute form of bulbar paralysis is relatively good if the patient survives the acute stage. In cases due to a supra-nuclear lesion the course of the disease is often prolonged. In infra-nuclear or extra-medullary cases the lesions are not infrequently syphilitic, and with suitable treatment the prognosis is good. It is, however, most difficult to distinguish between the symptoms due to a gummatous condition and those due to a new growth. In the latter condition the prognosis is, of course, very bad.

**Treatment.**—The acute cases should be treated by rest and careful feeding, and those due to syphilitic thrombosis of the vessels by the administration of iodides and mercury. Semi-solids are swallowed more easily than fluids, and have less tendency to pass into the air-passages. In the later stages quinine, iron, and strychnine may be given, and may hasten recovery. Electrical treatment is frequently employed, but it cannot be said to be of much service in these cases.

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## SYPHILIS OF THE SPINAL CORD AND ITS MEMBRANES

By WILFRED HARRIS, M.D., F.R.C.P.

THE period during which syphilitic spinal disease may ensue after the primary infection is usually within the first eight or nine years, though the more chronic forms of sclerosis and endarteritis may occur very much later, certainly forty years after the primary disease. It is not very uncommon to meet with cases of meningo-myelitis as early as six months after the acquirement of the chancre, and I have seen one case of acute paraplegia which appeared three months after infection. It has been stated that early syphilitic cerebrospinal affections are invariably the result of neglect of primary treatment. This, in the main, is undoubtedly true, though notable exceptions may occur, as in the case just referred to, a soldier who contracted syphilis in India. For three months he was treated continuously for the disease in a military hospital, but, on the very day of his discharge, a few hours after leaving the hospital, he became paraplegic, no doubt from a transverse myelitis, which had improved only slightly when I saw him twelve months later.

**Morbid Anatomy.**—The large majority of cases of chronic syphilitic spinal disease are due to invasion of the membranes, chiefly the pia-arachnoid, by a growth of granulation-tissue which produces thickening of the pial sheath and encloses both spinal roots and cord in the new formation, thus setting up a chronic meningo-myelitis. Before opening the dura the whole cord may appear uniformly swollen over a considerable length.



Microscopically, the meninges are much thickened, and infiltrated with small round cells, especially around the vessels. It would naturally be anticipated that this syphilitic material would contain the *Treponema pallidum*, but in the case described by Klippel and Dainville it was not found. Periarteritis is almost constant, and the lymphatic sheaths of the arterioles are distended with embryonic cells. The coats of the vessels are thickened by arteritis, especially of the middle coat, the lumen of the vessels is thus narrowed in places, and thrombosis often follows. In addition there may be a corresponding endo-periphlebitis with thrombosis. Besides this diffuse implication and thickening of the pia-arachnoid and its vessels, the intraspinal vessels may shew similar changes to those above described, and, as a consequence of the vascular disease, both meningeal and intra-medullary, various forms of sclerosis of tracts and even of nerve-cells are met with, in addition to acute myelitic foci which may occur apparently independently of actual endarteritis. Gummas too are not infrequent in the membranes, and around the roots, both anterior and posterior; and gummatous growths may also occur in the cord, usually in the white matter. These gummatous tumours of the roots and membranes may cause symptoms of spastic paraplegia by pressure upon the cord, and, according to Sir Victor Horsley, a chronic syphilitic infection may sometimes set up a localised serous meningitis, the accumulated cerebrospinal fluid causing serious compression and flattening of the cord (*vide* p. 617). Congenital syphilis may affect the spinal cord and membranes as in the adult, and may produce symptoms either soon after birth or in later life. (Myelitis due to syphilis is described on p. 659.)

The following five forms of chronic syphilitic spinal disease occur:—

1. **Chronic Meningo-myelitis.**—This is the commonest example of the more chronic forms of spinal syphilis. Usually commencing from two to eight years after the primary infection, it is generally preceded or accompanied by some signs of a cerebral lesion, such as hemiplegia, persistent headache, diplopia or other cranial nerve palsy, or Argyll Robertson pupil. Exciting causes which sometimes undoubtedly hasten the onset of the symptoms, or may even determine the commencement of the syphilitic formation in the membranes, are:—exposure to cold, injury, and the incidence of other infective processes, notably influenza.

*Symptoms.*—Pain in the limbs or back is the commonest initial symptom, and is usually worse at night. There may be darting, shooting pains in the legs and arms for some years, or the pains may be more of a boring character, like very violent knife-thrusts. The more rapid cases may run their course in from six to twelve months, the pains being followed by progressive weakness and numbness in the legs, and difficulty in walking. One leg is often much weaker than the other, and if the stress of the disease falls especially upon one side of the cervical or upper dorsal portion of the cord, the Brown-Séquard syndrome of weakness and spasticity of the lower extremity of the same side, and analgesia of the opposite limb, is comparatively common. The sphincters are generally affected as soon as there is any weakness of the lower limbs, retention of



urine and hesitation of the bladder being in most cases the first symptom. Incontinence appears later, and the anal sphincter may also become paralysed with incontinence of faeces, when the sacral region of the cord or the cauda equina is affected. When the disease is so far advanced that the lower extremities are practically powerless, with paralysis of both sphincters, the pains in the limbs may disappear, and progressive emaciation, fever, and frequent vomiting give warning of the coming fatal termination. The two most dangerous and common complications at this stage are cystitis, with secondary infection of the kidneys and sacral bed-sore. The latter may prove intractable, and increase in both area and depth in spite of all treatment and, ulcerating into the spinal canal, eventually cause death from purulent meningitis.

In other cases symptoms of intermittent claudication may be present in varying degree for many months before leading to more definite signs of cord injury. A slight blow upon the back from a fall, or a severe chill, may be followed by a numb feeling in the lower part of the back and darting pains in the limbs. Vague sensations of pins and needles and cramps in the legs may alternate with occasional hesitation of the bladder, or a girdle-sensation around the lower part of the trunk or referred to the perineum, backs of the thighs, or even around the ankle or instep. It is most important to recognise this stage, because intensive specific treatment may then prevent permanent paralysis. The condition of the reflexes varies according to the degree of invasion of, or pressure upon, the cord or the roots, both anterior and posterior. Usually the knee- and ankle-jerks will be increased, perhaps even to the extent of knee- and ankle-clonus, and the plantar reflex is extensor. In cases in which the lumbo-sacral roots are much affected the knee- and ankle-jerks may be absent, or very much diminished, though even then the Babinski sign of extensor plantar reflex may be quite well marked, and the forearm-jerks brisk. Absence of the deep reflexes is especially likely to be noted when the disease is nearing a fatal termination. Muscular wasting may be part of a general emaciation, or it may be local, due to implication of the anterior roots in the gummatous formation.

**Sensation.**—In addition to subjective sensations of numbness and pain, anaesthesia and analgesia of varying intensity may be found. Usually only slight and diffuse on the lower limbs and trunk, in some cases dissociated anaesthesia of the syringomyelic type may occur, with complete or nearly total analgesia and loss of the middle ranges of temperature sense, with tactile sensation almost unimpaired. In the most severe cases, especially in those with a sacral bed-sore, there may be complete anaesthesia of the feet, legs, and perineum.

**2. Lateral and Combined Sclerosis.**—In 1892 Erb described a form of syphilitic spinal paralysis, characterised by chronic weakness of the legs with increase of the deep reflexes, spastic gait, yet with hypotonus rather than muscular contractures, weakness of the bladder, and slight diminution of sensation in the lower limbs.

*Morbid Anatomy.*—According to Wimmer, in four published cases

only has a pure pyramidal degeneration been found, the more usual picture being a diffuse combined sclerosis of practically all the tracts in the cord. In some cases small focal myelitic lesions may be found, especially in the dorsal region, which could account for only some of the degeneration, and slight changes in the meninges and vessels. In Renner's case, a man of thirty-six, who for nine years had pains in the legs and cramps in the calves, developed four months before death spastic symptoms with ataxy, and later cystitis. There was also ataxy of the arms, Argyll Robertson pupils, optic atrophy, and a zone of diminished tactile sensation around the upper abdomen, phenomena suggesting tabes, though the knee-jerks were increased, and the plantar response extensor. The necropsy revealed changes in the cervical cord resembling those of incipient tabes superior, mainly of the postero-external columns, increasing upwards, with well-marked degeneration of the crossed pyramidal tracts, increasing downwards. There was not any thickening of the pia, nor any local meningitis or compression.

Since the peripheral white matter in the cord derives its vascular supply from the meningeal vascular network surrounding it, it appears highly probable that the majority if not all of the cases of syphilitic diffuse combined sclerosis are due to gummatous meningeal involvement, causing obliteration of the nutrient vessels from endarteritis and endophlebitis. In other cases in which ascending and descending degenerations start from a definite region of the cord, these have been shewn to be due to myelitic foci within its substance, secondary to vascular obliteration. Indeed, it is an open question if tract degenerations, such as those described above, are ever really primary and not due to a patch of syphilitic softening in the pons or elsewhere in the course of the involved tract, as in Dr. Gordon Holmes' case. If truly primary, they must be classed with tabes and general paralysis as metasyphilitic diseases.

*Symptoms.*—The disease, which is usually very chronic, is an incomplete paraplegia developing very gradually, with spastic ataxic gait. It may become arrested, the symptoms remaining unchanged for ten years or longer. The knee- and Achilles-jerks are much increased, with ankle clonus, and the Babinski sign of extensor plantar reflex. Combined with the spastic gait there is hypotonia of the lower extremities, an important diagnostic feature; bladder symptoms occur early, hesitation of micturition, with retention, and later incontinence. Pain in the back and legs is often a prominent symptom, and girdle-sensation may be complained of; numbness of the lower extremities and a slight general diminution of sensibility to touch and pain in this region, with no dissociated anaesthesia or distribution in spinal root or cord segmental area. In others no trace of sensory loss is to be detected. There is no muscular atrophy, and, except in rare cases, no involvement of the arms; and the eyes, pupils, and all the other cranial nerves are generally unaffected. Sluggishness of the pupils or even complete reflex iridoplegia may, however, be met with.

The cerebrospinal fluid obtained by lumbar puncture shews only a slight lymphocytosis and a trace of albumin.

**3. Spinal Gumma.**—As already mentioned, gummas may occur in the substance of the cord or in the membranes in diffuse syphilitic meningo-myelitis. Occasionally a single gumma in the pia-arachnoid may be large enough to cause pressure-symptoms by implicating the cord, the roots, or both. This may occur at almost any time after six months from the primary infection. The symptoms produced will be those of spinal tumour, and general indications of involvement of the cerebrospinal nervous system by syphilis may be entirely absent. In such a case gumma can only be provisionally diagnosed upon the history, but if besides the localising signs of pressure upon the cord and roots there has recently been severe nocturnal headache, diplopia, transitory aphasia or hemiplegia, or various paraesthesias, syphilis is much more likely to be the cause of the pressure-symptoms. Lumbar puncture and examination of the cerebrospinal fluid, and, if a definite history of syphilis is unobtainable, examination of the blood for the Wassermann serum-reaction, will confirm the diagnosis.

The rapidity of onset of the symptoms varies from several weeks to a few months. Pain in the back and limbs is usually the first feature, and may be regarded as rheumatic, though the usual anti-rheumatic treatment fails entirely to relieve. When the gumma is in the cervical region, the pains are in the neck, around the shoulder, and down the arm, whilst tenderness on percussion or pressure over the spine corresponding to the site of the gumma may be present. If the lesion implicates the anterior roots as well as the posterior, rapidly increasing weakness of the arm, with muscular wasting and coarse fibrillar tremors of the muscles, will be a prominent feature. The grouping of the muscular atrophy will distinguish the spinal lesion from a brachial neuritis or other lesion of the plexus, for instead of the affected muscles corresponding to the distribution of the peripheral nerves, the grouping of the muscular paralysis will represent spinal segments. Thus, the deltoid, spinati, flexors of the forearm, and the radial extensors of the wrist are liable to suffer together in a lesion of the fifth cervical segment of the cord; or, again, the serratus magnus, latissimus, triceps, and lower half of the pectoral will indicate the sixth cervical segment as the site of the gumma. When a gumma implicates the posterior roots, there will be anaesthesia as well as muscular wasting in the upper extremity, the anaesthesia, like the muscular paralysis, corresponding to the distribution of the spinal roots and not to that of the peripheral nerves. The pressure of the gumma upon the spinal cord is likely to cause symptoms of spastic paraplegia by indirect pressure upon the pyramidal tracts, though the two sides are often not affected to the same extent. When this is the case, the lower extremity on the same side as the affected arm will be the weaker and the more spastic, and the knee- and Achilles-jerks will be increased, with ankle-clonus and extensor plantar response. The abdominal reflex also on the same side will probably be diminished, though this is not invariable.



The Brown-Séquard syndrome, characteristic of unilateral lesions of the cord, will be present in many cases in a more or less perfect form. Often there is little or no tactile loss, though the analgesia and therm-anaesthesia may be profound, and usually the patients are quite unconscious of any subjective numbness of the skin and of any sensory loss, until it is demonstrated to them. An interesting point in those cases shewing crossed analgesia is that the upper level of the analgesia by no means corresponds to the level of the spinal lesion, as, for instance, the tactile anaesthesia in cases of fracture-dislocation of the spine definitely indicates the level of the compression of the cord. In two cases of spinal gumma, under my observation, with weakness and wasting of the left arm and spastic paralysis, mainly in the left leg, there was crossed analgesia of the right lower extremity only, extending as high as the right groin, but no sensory loss whatever on the left leg, abdomen, or chest.

The *treatment* of spinal gumma is much more hopeful than that of many cases of chronic meningo-myelitis or syphilitic combined sclerosis, in which there is present obliterative endarteritis rather than gummatous exudation. Energetic mercurial treatment, combined with the administration of iodide of potassium, may effect a complete cure though the iodide may have to be pushed in large doses. I have seen a case of this disease which made no progress while taking liquor hydrargyri perchloridi in dram doses with 15 grains of iodide of potassium, three times daily, begin to improve when the iodide was increased to 25 and later to 40 grains in each dose, the improvement continuing until the gait became normal and the weakness of the legs was scarcely noticeable.

**4. Chronic and Subacute Poliomyelitis.**—This is a rare but undoubted sequel of syphilis; three very definite examples have come under my notice, two within two years. Nonne (9a) describes 3 cases of subacute syphilitic poliomyelitis, in each of which the upper extremities alone were affected. J. Hoffmann has also seen 3 cases of chronic poliomyelitis in syphilitics. It generally appears to be mistaken for progressive muscular atrophy, though in one case the diagnosis of lead palsy had also been made, as the affected muscles were chiefly the extensors of the wrist and fingers. Pain is usually present at the commencement, around the shoulder and back, and the muscular paralysis is usually bilateral, though not absolutely symmetrical. Thus, in a woman, the first symptom was pain two years before in the left upper arm, followed by paralysis of the left deltoid. Twelve months later the right wrist became dropped, and soon the right shoulder became paralysed like the left arm. A year later there was almost complete paralysis of both deltoids, biceps, spinati, and of the extensors of the wrist and fingers on both sides. Electrical testing shewed well-marked reaction of degeneration in all these muscles; no sensory loss to touch or pin-prick anywhere. All the deep reflexes were absent, with the exception of the jaw-jerk, and the pupillary reflexes to light were very sluggish. In this case, which had been treated elsewhere for progressive muscular atrophy by injections of strychnine without any

improvement, the clue to the diagnosis of syphilis as the probable cause lay in the loss of the knee- and Achilles-jerks, together with pronounced sluggishness of the pupillary reflex to light. Nothing in her history supported this conclusion, but the Wassermann reaction for syphilis gave a very definite positive result. The chronic atrophy of the cells is probably due to obliterative endarteritis of the branches of the anterior spinal artery which supply the anterior horn. Spiller describes a case, with necropsy, of thrombosis of the anterior spinal artery from syphilitic endarteritis, causing acute poliomyelitis, with numbness and loss of power in all four limbs, affection of the sphincters, and marked sensory disturbances. Hoffmann also records a clinical case of acute poliomyelitis in a congenital syphilitic, aged twenty, causing atrophic paralysis of the right arm and left leg, loss of the deep reflexes, without any sensory or sphincter affection. The paralysis appeared acutely in one night, after a few weeks' premonitory pains in the right arm and in the back.

*Diagnosis.*—Complete or partial Argyll Robertson pupil has been present in each of my three cases of syphilitic poliomyelitis, and in each there was double wrist-drop and weakness of the deltoids and other muscles of the fifth cervical group. In one there was also loss of most of the deep reflexes, but no other symptom to suggest tabes. The grouping of the affected muscles according to their representation in spinal segments will distinguish the disease from a peripheral neuritis, whilst the more rapid onset and the presence of a well-marked reaction of degeneration will differentiate it from progressive muscular atrophy. Examination of the cerebrospinal fluid obtained by lumbar puncture is negative in these cases, as the meningeal reaction of excess of albumin and of lymphocytes is absent in this form of spinal syphilis.

*Treatment.*—Since the disease is probably due to a chronic or sub-acute atrophy of the anterior horn cells, and is a very late sequel of syphilis, in 1 of the 3 cases appearing twenty-five years after the infection, it is unlikely that antisymphilitic treatment would be of much, if any, avail in arresting or curing the disease. I have tried both antisymphilitic medication and injections of strychnine without notable improvement, though in one case the wrist-drop did improve considerably for a time under strychnine injections, afterwards relapsing into the same condition in which it appeared two years before.

5. **Gummatous Radicular Neuritis.**—This affection of the roots differs from a meningo-myelitis in that in the former the gummatous infiltration is confined to the roots, and does not invade the spinal cord. The symptoms will therefore be limited to the nerve roots, and there will not be any signs of pressure upon the spinal cord. The lumbar roots are in my experience the more frequently involved, the symptoms commencing with pains around the hip and in the thigh, which are liable to be regarded as sciatica or rheumatic. Wasting of the thigh muscles soon follows, with weakness of the limb, and indefinite numbness and slight analgesia of the front of the thigh and leg may also be found. Lavastine and Verliac have described a case in which a gummatous

meningitis involved all the sacral and the two lowest lumbar roots on the right side only, one-half of the cauda equina being thus damaged, the *syndrome de l'hémi-queue de cheval*. The symptoms were those of sciatic pain, paralysis of the leg, steppage gait, loss of the knee- and Achilles-jerks, and of the plantar and anal reflexes, retention of urine with constipation, anaesthesia to all forms of sensation on the foot and leg to just below the knee, and behind on the calf and thigh up to the gluteal fold.

*Prognosis and Treatment.*—This form of syphilitic neuritis is usually very amenable to treatment, and responds rapidly to energetic innunction with mercurv and iodide of potassium internally. Innunction with 10 per cent oleate of mercury, made up with lanoline, combined with liquor hydrargyri perchloridi in dram doses and increasing amounts of iodide of potassium, given internally, usually succeed in arresting the progress of the disease. Massage and faradism, or if the muscles are very much wasted, galvanism with slow reversals of the current, will complete the cure.

**Diagnosis of Chronic Syphilitic Spinal Disease.**—The diseases with which chronic syphilitic spinal disease is most likely to be confused are, disseminated sclerosis, tabes, combined sclerosis due to causes other than syphilis, spinal tumour or caries, and rheumatism and other causes of neuritis. The slow onset of the spastic paraplegia in chronic syphilitic meningo-myelitis and in Erb's syphilitic lateral and combined sclerosis, may be indistinguishable from the similar weakness of the legs met with in disseminated sclerosis and in combined sclerosis. Hypotonia, combined with greatly increased deep reflexes, extensor plantar reflex, and spastic gait, will be a valuable point to distinguish the syphilitic from the disseminated form of sclerosis, though the early affection of the sphincters and little or no signs of anaesthesia will be common to both. Pain in the back and limbs and headache, especially if worse at night, strongly suggest syphilitic disease. Diplopia and other signs of implication of the cranial nerves are common to both diseases, though third nerve palsy is as common a sequel of syphilis as it is rare in disseminated sclerosis. Argyll Robertson pupil in one or both eyes, whether the loss of the light-reaction is total or only partial, is almost, though not quite, pathognomonic of syphilis. The age and history of the patient will be of some help in the diagnosis: disseminated sclerosis is comparatively common in young unmarried women of twenty-five to thirty-five years of age, in whom there may be no reason whatever to suspect syphilis, whereas the larger number of sufferers from chronic syphilitic spinal disease will be men, and a history of antecedent infection may be obtained. The Wassermann serum-reaction for syphilis, in the modified form described by Dr. A. Fleming, has recently become readily available in practice, and valuable help may be obtained by this means in cases with a doubtful or negative history of syphilis. The test, although a valuable additional means of diagnosis, is not absolute in its certainty, and may give a negative result in cases of syphilis cured by long-continued treatment. On the other



hand, I have seen it positive in a case of juvenile tabes in a young woman of twenty-five, due to well-marked congenital syphilis. In a recent case of my own of syphilitic hemiplegia in a young man of twenty-five, Dr. Fleming found a positive reaction to the Wassermann test in the cerebrospinal fluid, whilst it was negative in the blood. (For a full consideration of the Wassermann reaction see p. 278.)

Well-developed tabes, with absent reflexes, ataxic gait, gastric crises, and so forth, is not likely to be mistaken for spinal syphilis; but the earlier stages of tabes, especially if the knee-jerks are not yet lost, may be difficult to separate from it. Definite signs of spasticity, such as the extensor plantar reflex, will be conclusive against tabes; but pains, loss of knee-jerk, Argyll Robertson pupil, anaesthesia, sphincter troubles, and implication of the cranial nerves are common to both diseases. Loss of the knee-jerk is less common than increase of the deep reflexes in spinal syphilis; and it has been asserted that those cases, diagnosed as tabes, which improve notably under energetic antisymphilitic treatment, are not really tabetic, but are instances of chronic syphilitic meningo-myelitis; and are called syphilitic pseudo-tabes. Of this view I am by no means fully convinced, and if Nageotte's view that tabes commences as a chronic syphilitic radicular neuritis and meningitis is even partially true, the argument falls to the ground (*vide* p. 744).

Some help in the diagnosis of spinal syphilis is afforded by the examination of the cerebrospinal fluid obtained by lumbar puncture. A large excess of protein, combined with the appearance of lymphocytes in the stained film after centrifuging the fluid, are the two points which will help to distinguish syphilitic meningo-myelitis from spinal sclerosis due to causes other than syphilis. Both these changes in the fluid are met with also in tabes and in general paralysis, and especially in the latter the lymphocyte count may be excessive. In syphilitic lateral and combined sclerosis, and in the form of subacute poliomyelitis above described, the cerebrospinal fluid will shew little or no change from the normal.

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## TABES DORSALIS

SYNONYMS.—*Locomotor Ataxia*; *Posterior Sclerosis of the Cord*.

By J. A. ORMEROD, M.D., F.R.C.P.

**Historical.**—Early in the last century certain German physicians had constructed a rough account of this disease, and Romberg in his *Text-book of Nervous Diseases* (1846) gave an authoritative description of it. In this country observations had been made by Stanley, Todd, and Gull, and in France by Ollivier and Cruveilhier; but out of Germany the disease had not been recognised as a uniform group of symptoms. Hence, when Duchenne's masterly clinical sketch appeared (1858) it was generally accepted as the description of a new disease. Duchenne, emphasising a fact on which Romberg had laid little stress, shewed that, while muscular power may be retained, the orderly performance of movements is increasingly impaired, and he therefore proposed the well-known name, "progressive locomotor ataxy." But the phenomenon of "ataxia," or "inco-ordination," had already been described by Todd, and associated by him with the sensory paralysis of the legs, and disease of the posterior columns of the cord. Thus Sir W. Gowers claims for Todd the discovery of the disease:—

"Two kinds of paralysis of motion may be noticed in the lower extremities, the one consisting simply in the impairment or loss of the voluntary motion, the other distinguished by a diminution or total loss of the power of co-ordinating movements. In the latter form, *while considerable voluntary power remains*, the patient finds great difficulty in walking, and his gait is so tottering and uncertain that his centre of gravity is easily displaced." He states that the cases are chronic, and in two examples of this variety of paralysis (sensory) he predicted disease of the posterior columns, and such was found to exist on post-mortem examination.

Nevertheless, Duchenne's writings, backed by the authority of Troussan, obtained for the disease a wide recognition, and both clinical and pathological records became more general. Thus important observations were made by Charcot, Vulpian, Bouehard, and others; monographs upon it appeared also, such as those by Topinard in France and von Leyden in Germany. Among English physicians Dr. Hughlings Jackson wrote particularly on the optic atrophy, and Lockhart Clarke on the morbid anatomy. On this latter subject Pierret began a series of papers in 1870, pointing out a special part of the posterior columns as the starting-point of the spinal lesion. A few years later came Charcot's famous lectures, which awoke much interest both in this disease and in the subject of

nervous diseases generally. In these he dwelt particularly on certain less-known symptoms, such as the joint disease (which had been previously described by him), the visceral crises, and so on. Accounts of the articular symptoms were also published by Sir Clifford Allbutt (1869) and by Dr. T. Buzzard. In 1876-78 Erb published his well-known article in von Ziemssen's *Encyclopaedia of Practical Medicine*, ably setting forth the whole subject of tabes.

The phenomena of tendon-reflexes, simultaneously broached by Westphal and by Erb in 1875, gave a fresh impulse to the study of this disease; since by Westphal's sign (loss of knee-jerk), and by Argyll Robertson's sign (loss of the pupillary reflex under the stimulus of light), we are enabled to diagnose its early stages with far greater precision. From that time an ever-growing number of observations has appeared, among which I may specially mention divers interesting clinical histories by Dr. T. Buzzard; statistics on the relations of syphilis to tabes by Fournier, Erb, and others; observations on peripheral nerve degeneration in true tabes by Pitres and Vaillard, and by Oppenheim; the simulation of tabes by peripheral neuritis (pseudo-tabes) by Dejerine; the article upon tabes in the *Textbook of Nervous Diseases* by Gowers, the lectures upon the subject by Marie, the Lumleian lectures on tabes, delivered by Dr. Ferrier before the Royal College of Physicians in 1906, and the studies by Dr. Mott of the relations between tabes and general paralysis, and between both these diseases and syphilis.

**Etiology.**—Almost all physicians are now agreed that the chief cause of tabes is syphilis. This view originated in statistics, which shew that syphilis is an antecedent so common that we can hardly avoid including it in the causation. Other data are being gradually collected which point in the same direction, such as the occurrence of conjugal tabes, and the condition of the blood-serum and of the cerebrospinal fluid (*vide*, p. 746). So that in the opinion of some authorities syphilis is ranked as a *sine qua non*; "no syphilis, no tabes," is a sweeping statement which may be true, but is a little hard to prove completely. How syphilis produces tabes is a difficult question, not yet fully settled, which will be best discussed after the consideration of the morbid anatomy; but all are agreed that tabes is not a gummatous affection of the nerve centres, such as could be removed by mercury or iodide, but a remote effect (para- or meta-syphilitic), for which past syphilis has laid the foundation.

Another great factor in the etiology is *sex*. Men suffer in a far larger proportion than women. The reason of this we do not know, nor how to reconcile it with a purely syphilitic etiology. As to *age*, the disease commonly manifests itself first in the fourth or fifth decade of life, though there may be exceptions to this, and a close inquiry into early symptoms may carry its origin farther back than was suspected. But probably the date of onset depends upon the age at which syphilis has been acquired rather than upon the actual age of the patient. The average interval between the infection with syphilis and the outbreak of tabes is given by Dr. Ferrier as seven to ten years, by Dr. Mott as eight



to fifteen years; but, doubtless, it may exceed or fall short of these limits.

Cases of true tabes occurring in *children* or young people, "juvenile tabes," are extremely rare, rarer than the corresponding juvenile general paralysis. They have to be distinguished from Friedreich's ataxia on the one hand, and on the other from gummatous disease of the nerve centres and meninges, which may arise in the course of congenital syphilis. In juvenile tabes, optic atrophy is said to be unusually common, but marked ataxia of gait rare. I am not aware that the diagnosis has, as yet, been verified post-mortem. There is usually evidence of syphilis, either accidentally acquired or congenital, or at least evidence that the parents have had syphilis. In a considerable proportion of such cases, a parent has suffered not only from syphilis but also from tabes (or general paralysis), suggesting that in such instances there may be an hereditary proclivity to the disease. But in ordinary tabes, as seen in the adult, *heredity* does not appear as an etiological factor. There may sometimes indeed be a "general nervous heredity," that is to say, nervous diseases may figure largely in the patient's family history, but the disease itself is not transmissible, nor is it in any sense a "familial" disease. Conjugal tabes must here be noticed, *i.e.* cases in which a husband and wife have suffered from tabes or general paralysis. The disease is sufficiently uncommon in women to make it unlikely that this was a pure coincidence, and there has been in such cases a history of syphilis affecting the pair, which in all probability gives the clue to the origin of the tabes.

Turning from general and remote influences to proximate and determining causes, we find the following enumerated: exposure to cold; over-exertion, especially when combined (as in military campaigns) with exposure and privation; sexual excess; trauma. Sometimes the history reveals none of these things, sometimes one of them assumes such prominence as to convince the patient at any rate of its importance. Their proper estimation is difficult, and necessitates careful inquiry into the circumstances of each case, for early symptoms, forgotten or disregarded, may have preceded the action of the supposed cause, which may have merely aggravated but not initiated the disease. This applies particularly to histories of *injury* causing either a general shock or a shock to the spine, such as blows, falls, railway collisions. A patient may become ataxic after such an injury, but we must not assume that his disease originated in this way till we have learned that there is no previous history of lightning pains, squint, or other early symptom of tabes. But there may be another sequence of events. An injury to a limb is followed by lightning pains, which begin at the seat of injury and subsequently become generalised, the other phenomena of tabes appearing in due course. The relation of cause and effect seems at first sight clear; and the explanation generally given is that a neuritis was set up which spread upwards by the posterior roots into the cord. However, the possibility of such an extension seems rather doubtful; and Hitzig, from an analysis of such cases, concludes that there are very few which, even

from the clinical side, are above criticism. On *sexual excess* a traditional stress has been laid; among modern and independent writers Erb ranks it as a factor in the etiology of tabes. It is obviously a difficult subject for inquiry, and the more so as abnormal sexual excitement has been reckoned among the early symptoms of the disease.

I incline to the view that there is in all cases some remote influence, which is generally past syphilis, or in some few cases other factors as yet unknown; and that upon this may follow the nerve degeneration, either without definite proximate cause, or determined by some of the proximate causes we have just enumerated.



FIG. 82.—Photomicrograph of a transverse section of the posterior root (3rd lumbar) from a case of advanced tabes. The small dark round bundle of fibres is the undegenerated anterior root, the large sclerosed root is the posterior. Section stained by Weigert's method. Magnification, 20 diameters. (Mott.)

**Morbid Anatomy.**—Tabes is a primary progressive degeneration of the first afferent (sensory) projection-systems of neurons, by which peripheral sensations are cut off from various parts of the central nervous system; the commonest and most obvious anatomical change being degeneration of the posterior spinal roots and the posterior columns of the spinal cord.

After opening the spinal canal and slitting up the dura mater, it will be observed that the pia-arachnoid is thickened over the posterior surface of the cord, which is flattened, and presents a greyish or greyish-red aspect; moreover, the posterior roots are thin, flattened, and atrophied, although the degree of wasting is not necessarily uniform; they also

present a grey appearance like the posterior surface of the cord. On removing the cord, and cutting it transversely, the degeneration is found to be limited to the posterior columns which are considerably shrunk, and of a greyish or greyish-red colour, contrasting strongly with the white antero-lateral columns. This degeneration is usually much more obvious and advanced in the posterior columns of the lumbo-sacral region; likewise the posterior roots entering into the formation of the cauda equina are, as a rule, atrophied to a greater degree than elsewhere. Normally the posterior roots are two or three times as large as the anterior; but in advanced cases of tabes they may, in the process of degeneration, waste to such a degree as even to be smaller.

The degenerative process, however, is not limited to the afferent spinal projection-systems; various cranial nerves may be atrophied. The grey atrophy of the optic nerve is obvious to the naked eye, and the peripheral nerves in many cases may exhibit degenerative changes.

*The Nature of the Degeneration.*—Microscopical examination of the spinal cord shews the myelin sheath of the nerve-fibres diminished or destroyed; the axis-cylinder process may be swollen in one place, attenuated in another, and generally irregular in thickness or completely atrophied; the neuroglia is increased at the expense of the parenchyma, and a large number of Deiters' cells are visible. Nearly the whole of the posterior columns in the lumbo-sacral region may be destroyed, leaving only the cornu-commissural and oval areas of endogenous fibres. The walls of the vessels are often thickened in the sclerosed area, and not elsewhere; this change is secondary to the degeneration, not causal; there is hyaline degeneration of the media; sometimes the vessels are so much thickened by this degenerative process as to become almost obliterated, especially when the sclerosis is advanced. The pia-arachnoid membrane is also thickened, and often presents the appearances of chronic inflammation.

*Distribution of the Degeneration within the Cord.*—Minute examination shews that the spinal degeneration in tabes corresponds to the intraspinal distribution of the posterior nerve-roots. These roots, on entering the cord, divide into ascending and descending fibres. Of the descending fibres we have not much precise knowledge. The ascending fibres divide into two primary groups, as follows: (a) A tract of fine fibres runs directly upwards at the tip of the posterior cornu, probably sending off branches into the cornu as it ascends. This is known as the tract of Lissauer, who shewed that it may degenerate in an early stage of tabes. (b) A bundle of fibres, some coarse, some fine, enters the cord on the mesial side of the posterior cornu, where it forms in transverse section a border between the posterior edge of the cornu and the remainder of the posterior column ("root-entry zone"). This bundle, as it ascends, quickly loses many of its fibres, which enter the grey matter and arboresce around the cells which are found therein. Some of them are quite short, since they enter the grey matter almost at once. These short fibres come into relation with the large cells of the anterior cornua, with



the cells of the posterior cornu, and possibly with those of the intermedio-lateral tract. Degeneration of the fibres connecting the posterior roots with the anterior cornua would account for the loss of reflex tone in the muscles, and for the loss of the knee-jerk, owing to interruption of the reflex arc at this point. A second set of fibres which ascend from the bundle forming the root-entry zone (in the lower parts of the cord) are of a medium length; they ascend for a certain distance, and then enter the grey matter to be distributed, as terminal fibrils, around the cells

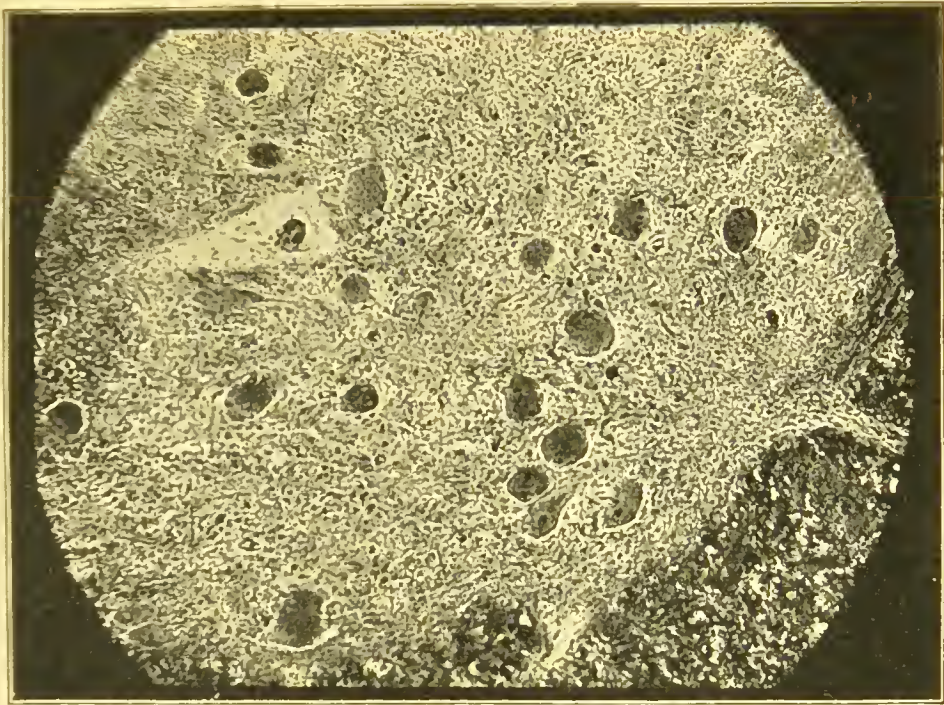


FIG. 83.—Photomicrograph of Clarke's column at the level of the 1st lumbar segment, from a case of tabes. There is complete atrophy of the fibres of the postero-external column, which break up into a brushwork around the vesicular cells. The cells themselves are unchanged, only the felt-work of nerve-fibrils which surrounds them is atrophied. Impulses from the periphery are thus cut off from the cerebellum. The axis-cylinder processes of these cells form the cerebellar tract. Magnification, 200 diameters. (Mott.)

of Clarke's columns. The degeneration, in tabes, of these fibrils has been demonstrated by Dr. Mott (Fig. 83). Since Clarke's columns are the point of origin of the ascending cerebellar tracts, this degeneration cuts off a route for afferent impulses from the posterior roots to the cerebellum, and (it is reasonable to suppose) may thereby give rise to disturbances of equilibrium. Lastly, when the short fibres and the medium fibres have left the posterior-root bundle thus to terminate around the cells of the grey matter, there remain certain long fibres which run all the way up the cord to the nuclei at the dorsal aspect of the medulla (nucleus gracilis, nucleus cuneatus), whence further relays of fibres provide a path upwards to

the cerebrum. By these three routes, therefore, the posterior-nerve roots are brought into connexion with all the main parts of the nervous system (Fig. 84). But the long fibres, as they ascend in the cord from the point of entry of their posterior-nerve root, gradually shift their position. They are pushed towards the middle line and backwards by the nerve-roots above them, each of which enters successively in the same way, viz. at the inner border of the posterior cornu. So that in the upper parts of the cord the long fibres coming from the lower nerve-roots occupy the

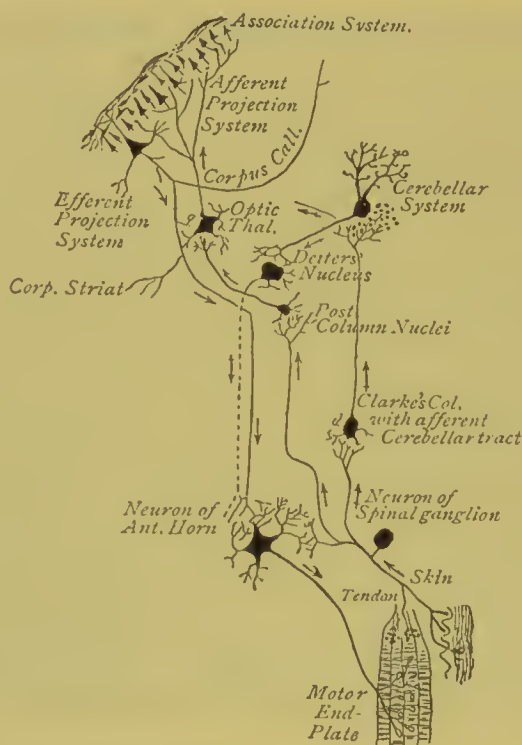


FIG. 84.—Diagram illustrating the afferent, efferent, and association systems of neurons. It will be observed that there are three nervous circles. In voluntary movements impulses are travelling along all these systems. In tabes there is degeneration and interruption of the afferent path in spinal, cerebellar, and cerebral systems; consequently inco-ordination of voluntary movements. Diagrammatically the posterior spinal ganglion is represented as giving off three processes; more probably it only gives off one. (Mott.)

posterior median columns (columns of Goll), and those which come in at higher levels occupy successively a position farther and farther from the middle line (till they are limited to the columns of Burdach).

In early stages of tabes, when only one or two roots are affected, a stripe of degeneration may be seen, on transverse section, in the posterior column, which was described long ago by Pierret under the name of the "bandelette" or "ruban externe." He described it as a narrow band skirting the internal aspect of the posterior horn, but separated from it by healthy white substance. This represents a posterior root bundle which has been partially displaced towards the middle

line by the entry of healthy roots above it, but before it has parted company with all its fibres which proceed to the grey matter. The degeneration of this stripe may be conspicuous when there are healthy fibres remaining on either side of it.

From what has been said concerning the intraspinal distribution of the posterior-nerve roots, it is clear that the morbid appearances to which tabes gives rise may differ considerably in different cases according to (1) the position of the nerve-roots involved, (2) the number of roots involved, (3) the completeness of the degeneration. Thus, in the rare

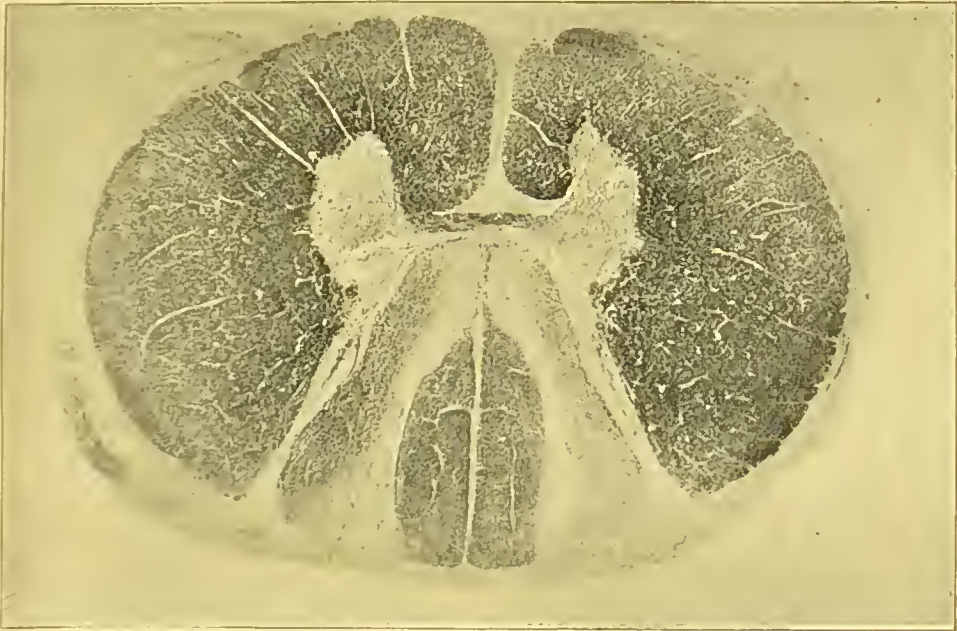


FIG. 85.—Cervical tabes. Section at the level of the 3rd cervical root. The lesion is asymmetrical; whilst on the left there is only ascending tabetic degeneration, on the right there is also local degeneration. The middle radicular zone contains fewer fibres than on the opposite side. The posterior-median columns are intact, as they consist of the healthy sacro-lumbar and dorsal root fibres which enter into the formation of Goll's column. (After Marinesco.)

cases known as cervical tabes (Figs. 85, 86), in which the disease attacks the cervical roots rather than those below, we shall find that in the upper parts of the cord the columns of Goll are healthy and the columns of Burdach degenerated, whilst in the lower parts of the cord the posterior columns are healthy in their whole extent. But in the usual form of the disease in which the lower nerve-roots, and many of them, are diseased, the lumbar and dorsal regions of the cord shew extensive degeneration of the posterior columns involving the whole cross-section, whilst in the upper parts of the cord, where healthy nerve-roots have come in, only the columns of Goll will be degenerated. Yet even in advanced cases certain small tracts of fibres may still remain intact, namely, those fibres which are considered to be "endogenous" (arising within the cord

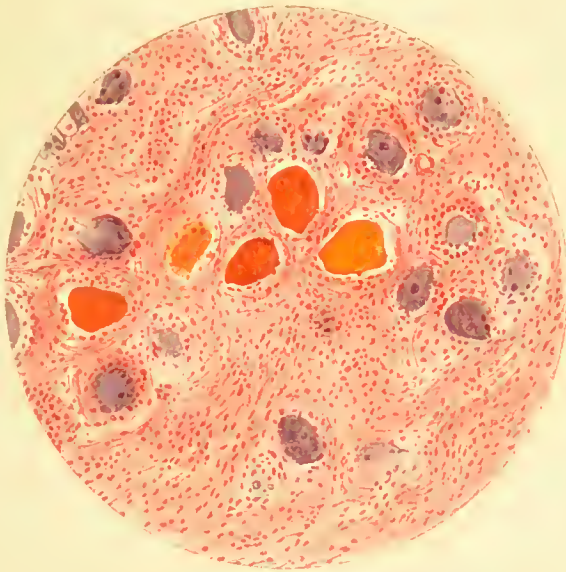


itself and not prolongations of nerve-roots). Thus we do not find degeneration in the "cornu-commissural zone," a tract which lies immediately behind the posterior commissure, and extends a little way along the inner edge of the posterior cornu; nor as a general rule in the fibres which, starting in the cervical and dorsal regions as the "comma tract," appear in the lower dorsal region as the "septo-marginal tract," in the lumbar region as the "oval field of Flechsig," and in the sacral region as the "median triangle" (Figs. 87, 88).



FIG. 86.—Cervical tabes. Section at the level of the 5th cervical. The same asymmetry of degeneration is observed in the posterior external columns, and Goll's column is intact. (After Marinesco.)

**Pathology.**—*Origin of the Degeneration.*—The distribution of the degeneration within the cord, selecting as it does a special system of nerve-fibres and leaving their neighbours intact, is sufficient to shew that it originates in the nerve-tissues themselves, and that the nervous degeneration is not secondary, as has been formerly supposed, to overgrowth of the neuroglia or disease of the vessels. These latter factors occur, but they are the consequences not the causes of the nervous disease. But how, and at what point of the posterior-root system does the degeneration begin? It is natural to think that it should begin in the ganglia of the posterior roots, since the cells of these ganglia are the trophic centres of the whole posterior-root system. Yet structural disease of these ganglion-cells, demonstrable microscopically, does not appear to be the rule. Some observers have found slight changes, others none; nothing at any rate has been found comparable to the changes in



Drawing from a photomicrograph of a spinal ganglion in a case of combined sclerosis of the posterior and lateral columns. The microscopical specimen was stained by Strömbö's method. The normal cells are purple, the degenerated cells are red. This red staining is due to a pigmentary degeneration of a fatty nature, for other sections stained by Papanicolaou's method show these same large cells stained purple. Examined with a high power, the cells are seen to be permeated throughout with the highly-refractive granules. In many of the cells the nucleus has disappeared. A similar condition of the cells was observed in a case of tabes, but not so pronounced. It is possible that this change may be due to terminal infection. Macintosh 200. (Mott.)





progressive muscular atrophy, in which definite disease of the anterior cornual cells is invariably associated with the wasting of muscle and efferent nerve fibre. Concerning the changes in the posterior-root ganglia, Dr. Mott, in the first edition of this work (Vol. VII. p. 107, 108), wrote as follows: "Atrophy and degenerative changes in the cells of the spinal ganglion have been described by Stroebe, Wollenberg, and others. I have myself examined—by Nissl, Stroebe, and Pal methods—4 cases of tabes, 2 of which were general paralytics, in which there was very advanced posterior-root degeneration (Fig 82), as well as almost complete

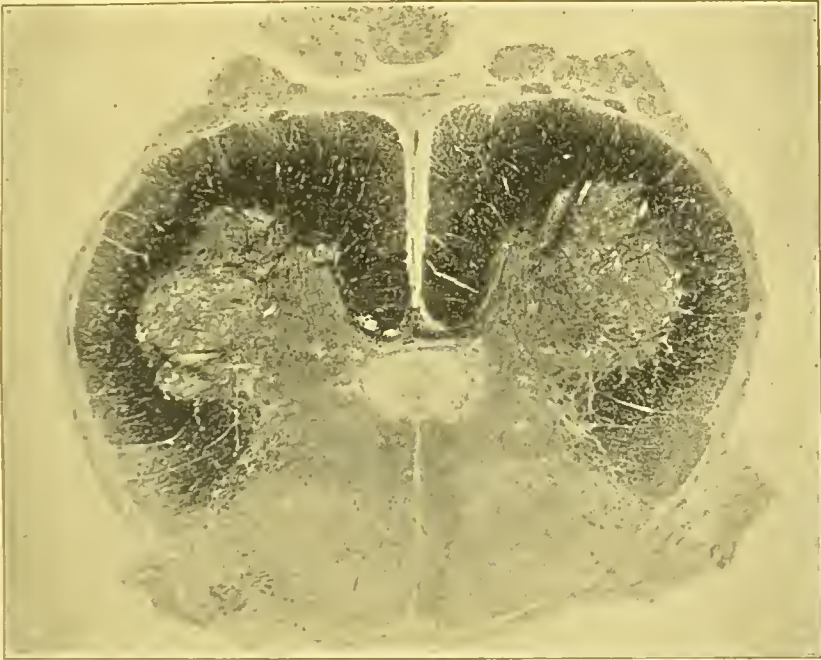


FIG. 87.—Photomicrograph of a section of the spinal cord at the level of the 5th lumbar segment, from a case of advanced tabes. There is a complete degeneration of the exogenous fibres of the posterior columns. In the middle line two oval areas can be seen which still contain undegenerated fibres of endogenous origin. The root-fibres entering the posterior horn are entirely destroyed, and the posterior roots are completely sclerosed. (Mott.)

sclerosis of the posterior columns (Fig. 87). In 2 cases all I could find were increase of pigment in the ganglion-cells, nuclear proliferation in the capsule and interstitial tissue, and sometimes vascular congestion; generally speaking, there was inflammation of the loose connective tissue surrounding the ganglion. In another case, one of advanced tabes, I found by Nissl's method, as well as the changes above mentioned, some apparent atrophy of the cells in the 4th and 5th lumbar spinal ganglia. Some of the sections shewed a few groups of cells in a state of advanced degeneration, the capsule either empty or containing only a little mass of pigment. In a case of sclerosis of the posterior columns, combined with lateral sclerosis in a syphilitic patient, a number of the cells stained

intensely purple by Pal and red by Stroebe method (*vide* Plate VI.). These cells had undergone fatty degeneration, and the nucleus was no longer visible. I have seen similar appearances in the ganglia of a case of tabes, but not so marked. It is therefore probable that the ganglion-cell is the last portion of the neuron to die, and that the process begins in the terminal twigs and spreads backwards to the body of the cell, but with greater rapidity in the central projection than the peripheral."

Other authors suppose that the spinal degeneration originates in disease of the meninges, affecting the spinal roots at certain points where they are peculiarly vulnerable. One such point, according to



FIG. 88.—Photomicrograph of a section of the spinal cord at the level of the 8th cervical segment, from a case of tabetic general paralysis. There is advanced sclerosis of the posterior columns. The cornu-commissural fibres of Westphal, endogenous in origin, are seen to be undegenerated. (Mott.)

Nageotte, lies where the posterior root pierces the dura mater, and receives, in common with the closely adjacent anterior root, a sheath of connective tissue from the dura and arachnoid. A chronic meningitis, which is a possible occurrence in a syphilitic subject, might give rise to a transverse neuritis at this point, and so start a degeneration in all the ramifications of the nerve-root. The objections to this hypothesis are, first, that the existence of such a meningitis, at least as a necessary antecedent of tabes, has never been proved, and secondly, that the adjacent anterior root would almost certainly be involved as well, so that muscular atrophy in tabes ought to be the rule instead of being, as it is, the exception. Another vulnerable point, according to Redlich and Obersteiner, is at the

entrance of the posterior root into the spinal cord. Here the enveloping pia mater is said normally to form a constriction around the entering nerve-root (ring of Obersteiner), and to cause a narrowing of its calibre, so that if any inflammation of the pia took place, it might result in additional constriction, thus injuring the nerve-root and consequently its intraspinal ramifications. As regards the supposed meningitis, the same objection holds here as in the case of Nageotte's view, namely, that its existence as an early factor in tabes is hypothetical. Still it certainly seems possible that there are other processes short of an actual meningitis which may affect the posterior-root system where it enters the cord. It is here that the nerve-fibres lay aside their sheath of neurilemma, the presence of which distinguishes peripheral nerve-fibres from those of the central nervous system. And whether it be for this reason, namely, the denudation of neurilemma, or whether it be, as maintained by Marie and Guillain, on account of peculiarities in the lymph-circulation of the posterior columns which bring it here into special relation with the lymphatic spaces of the meninges, it seems probable that the point of entry of the posterior roots may afford a ready channel for disease entering from the meninges. And we know from recent researches that, though there be no actual meningitis, yet the cerebrospinal fluid presents abnormalities, even in cases of early tabes (*vide* p. 747). But all such hypotheses take too narrow a view of the pathology of tabes. For though the disease affects principally the posterior-root system of the cord, it is by no means limited to it. In the first place degeneration of the peripheral nerves supplying the skin, bones, joints, and so forth, has not unfrequently been found. The afferent fibrils of these nerves are, like the posterior-root system of the cord, derived from the cells of the posterior-root ganglia; the three structures form one neuron; whereof the cell is the nutritive centre, the fibres, peripheral and central, are the dendrons and axons. What we witness therefore in tabes is the gradual death of this neuron, beginning in the branches of the tree, usually the intraspinal branches, but sometimes also the peripheral branches, and gradually reaching the cell which is their root. Secondly, other afferent nerves may be affected. Atrophy of the optic nerve is a common, and often an early, occurrence. Atrophy of the olfactory nerve has been described by Pierret, and of the auditory nerve by Strümpell. The ascending root of the fifth, the fibres of which spring from the Gasserian ganglion, has been found sclerosed in a case in which there were symptoms during life pointing to affection of the fifth (Oppenheim). Likewise the solitary bundle which consists of afferent vagus and glosso-pharyngeal fibres was found sclerosed. Dr. Mott has found partial sclerosis of this bundle in a case of cerebro-bulbar tabes in which during life there was loss of taste. Lastly, other parts of the nervous system may be involved over and above the afferent apparatus. In some cases slight changes have been described in the cerebral cortex, corresponding to slight mental impairment, and there are the striking instances in which long-standing tabes terminates in general paralysis. There are evidences



that the disease may attack the efferent nerve structures—the frequent motor paralyses, the hemiatrophy of the tongue, the progressive ophthalmoplegia due to degeneration of the oculomotor nuclei, the (less common) generalised muscular atrophy due to degeneration of the anterior cornual cells. (For the condition of the sympathetic see p. 498.) All these considerations indicate that the morbid process in tabes is of a general nature and of wide distribution, rather than a local, and, so to speak, accidental lesion of the posterior-nerve roots. And even as regards the spinal lesion itself, its symmetry and its steady upward march point in the same direction.

The doctrine which seems best to explain this wide incidence of the disease seems to be that syphilis produces a toxin which may act on the nervous system in general, but has a primary and particular action on the posterior-root neurons. In favour of such a hypothesis may be quoted the analogy of certain post-febrile and toxic paralyses. As diphtheria causes a poison to be elaborated which, acting on the nervous system, produces post-diphtheritic paralysis, and as certain poisons, such as ergot or lathyrus, have a selective action on various strands of the spinal cord, so possibly may the nervous system and the posterior-root system in particular be poisoned and degenerate as the result of bygone syphilis. But there are certainly points in which this analogy fails. Between the syphilis and the onset of the tabes there is a long interval to be reckoned in years. Can we suppose that during all this time a poison is either latent or is maturing? Again, post-febrile paralyses have a tendency to recovery, they have not the chronic progressive character of tabes. It seems likely, therefore, that the conditions necessary for tabes include not only the poison of a disease like syphilis, but also something in the nature of the tissues themselves; a view put forward by Dr. Mott (in the first edition of this work) as follows: "It is probable that systemic degenerations are due to a progressive defective metabolism in the neuron itself. . . . It must be remembered that the nerve-cell is a perpetual element—it is incapable of regeneration; unlike the cell of a gland, its restoration is impossible. Consequently, a poison like syphilis may lower the vitality and diminish the durability of certain systems of neurons, and given stress, injury, cold, or sexual excesses as immediate factors, the balance of repair and waste is overturned, and the neurons die gradually and prematurely." In other words, the syphilitic poison does not directly destroy the nervous tissues, but saps their power of nutrition. And if the incidence of tabes after syphilis is not alike upon all individuals, nor alike for the two sexes, the reason for this may lie, partly in their different liabilities to the stresses and strains of life, partly in innate differences of vitality and powers of recuperation.

**The Cerebrospinal Fluid in Tabes.**—Since the introduction of lumbar puncture the cerebrospinal fluid in tabes has been carefully studied, with important results. It may be abnormal in three ways: (*A*) As regards its cell-contents. The normal cerebrospinal fluid is clear and contains

very few cells of any kind. Excess of lymphocytes occurs in syphilitic meningitis and active syphilitic disease of the central nervous system when this affects such parts as the cortex cerebri or periphery of the cord which abut on the meninges; it is very common in tabes and general paralysis, and may occur in an early stage of either, so that it may be a considerable aid to diagnosis, for in the majority of other chronic nervous diseases it is not very often present. The lymphocytosis in these two parasymphilitic diseases differs, we are told, from that of genuine syphilitic disease of the nervous system in this respect, that treatment by mercury does not materially reduce it. In a series of fifteen patients with tabes, Dr. Purves Stewart found the lowest count was 14 cells per c.mm.; the highest, 477; the average, 125.

(B) The fluid often reacts positively to Wassermann's test. For the details and rationale of this complicated process we must refer our readers to p. 278. The test has been extended to the cerebrospinal fluid, with the following results: (1) In cases of syphilis, in which the nervous system is not affected, the blood-serum reacts positively, the cerebrospinal fluid is negative. (2) Where syphilis involves the nervous system the general rule is as in (1), that is to say, the blood-serum reacts positively, the cerebrospinal fluid is negative. But there may be exceptions, and this part of the subject requires further investigation. (3) In parasymphilitic degenerations of the nervous system, such as tabes and general paralysis, the cerebrospinal fluid often reacts positively. Many more cases of general paralysis have been examined than of tabes, and it is highly desirable that more observations should be made in tabes. In the large majority of cases of general paralysis, roughly speaking 90 per cent, the serum and cerebrospinal fluid both react positively. In tabes the results are not so high, but we may say (again roughly) that the serum reacts positively in 75 per cent, the cerebrospinal fluid in 50 per cent. Plaut's figures are higher; he found that in general paralysis the blood-serum was always positive (and if it is negative, he thinks that general paralysis may be excluded), whilst the cerebrospinal fluid was positive in all but 8 of 147 cases. In tabes he examined the serum in 14 cases and found it positive in 11 (79 per cent), and the cerebrospinal fluid in 11 cases, finding it positive in 7 (64 per cent). The notable point at any rate seems to be that in both these diseases something appears in the cerebrospinal fluid, demonstrable by means of the Wassermann reaction, which so far as we know at present has been found only in the serum of syphilitic patients. This is important both as an assistance to the diagnosis of tabes and general paralysis, and as an additional argument in favour of their connexion with syphilis.

(C) Lastly, the cerebrospinal fluid in these two diseases contains an excess of protein, a form of globulin. It has been suggested that this may be the "something" on which the success of the Wassermann reaction depends. Should this prove to be so, we may hope that simple clinical tests may take the place of the complicated biochemical reaction, and that our knowledge will extend in proportion as methods become easier.

**Symptoms.**—An ordinary case of tabes falls naturally into three stages, according to the degree of intensity in the principal symptom—*inco-ordination*. In the first, sometimes called the *pre-ataxic stage*, there is no *inco-ordination*; the patient can stand and walk normally. In the second stage standing and walking are rendered more or less difficult. In the third the patient cannot stand or walk alone.

Probably the earliest symptom to attract the patient's attention will be pain. Of this there may be various kinds, but the most characteristic are the so-called *lightning pains*. These are sharp and shooting in character, sudden in onset, momentary in duration; they occur in bouts which last a variable time, which are *paroxysmal* (leaving intervals, it may be long intervals, of freedom), or which may be *periodic*. The general character, then, of the pains is *neuralgic*; but they are not, like *neuralgia*, necessarily limited to special nerve districts; they may haunt one spot, may be widely distributed, or may shift their seat rapidly. Usually the earliest pains are in the lower limbs; but this is not invariable, they may begin in the face or head. They are generally aggravated by damp or by cold winds, so that the patient calls them "*rheumatics*." They may leave a transient *cutaneous hyperaesthesia*. Sometimes in connexion with lightning pains, and sometimes without them, a sudden giving way of the legs has been noticed. There may be pain, too, that is not lancinating, but has a dull aching or boring character, and is situated in the back, trunk, head, or limbs. Many are the comparisons made by the unfortunate patients in whom the pains are severe: "like knives, needles, electricity"; "like ginlets, corkscrews, or hot irons thrust into the flesh"; "like wild beasts gnawing," and so on.

A history of causeless *paroxysmal shooting pains* should of itself direct our thoughts towards *tabes*; but other complaints may be made. These, as we shall see, may be very variable, but some are particularly common: for instance, *diplopia*, *squint*, or *ptosis*, depending on some transient *oculomotor palsy*; or difficulties of *micturition*, so that the patient either cannot pass water readily, or (which is perhaps more frequent) cannot retain it properly; the urine escapes from him involuntarily, or he has to hurry when once he has felt the desire to *micturate*. There may also be troubles in the genital sphere; or in walking the patient may experience a sense of fatigue quite disproportionate to the exercise.

Luckily the diagnostic importance of such complaints can be tested by physical examination, and for this we turn to the state of the *knee-jerks* and the state of the pupils. I need not now dwell on the method of investigating the *knee-jerk* and of the general inferences to be drawn from it. Suffice it to say that in *tabes*, even at an early stage, the *knee-jerk* is commonly absent, while the power, nutrition, and electrical reactions of the extensor muscles of the knee remain normal. This disappearance of the *knee-jerk* in *tabes* has been called *Westphal's sign*. The date of its disappearance we cannot usually fix; in some few cases the *knee-jerk* may disappear under observation,



becoming feeble, unequal on the two sides, and finally absent; in some few it may remain present for years; in some an early stage of exaggeration has been reported; but as a rule, when the patient first presents himself it is gone. It is to be noticed that the ankle-jerk also disappears, and even at an earlier stage (it is said) than the knee-jerk.

The symptom derivable from the *pupil* consists essentially in this—that the pupil does not contract (as normally it should do) when light is suddenly thrown upon the eye; but the normal contraction still takes place when the patient fixes a near object (that is, accommodates or converges). This is known as reflex iridoplegia, or as Argyll Robertson's sign. Commonly the pupils are small—sometimes so small as to deserve the name of “pin-point pupils,” and symmetrical with each other, both in size and in mode of action. Inequality in size, however, is not very uncommon, though unilateral reflex iridoplegia is decidedly rare. It is said, too, that such pupils do not dilate under the stimulus of pain. Varieties of action occur; thus, a pupil may contract to light, and then re-expand though the illumination be still maintained; probably this marks an early stage of reflex iridoplegia. Not infrequently, also, the pupils react neither to light nor to accommodation. The date of the appearance of the pupil sign is as difficult to fix as that of Westphal's sign. In some cases it may not appear at all, the pupillary reactions remaining normal; but on the whole it is a very uniform, trustworthy, and early symptom.

The combination of these three symptoms—lightning pains, loss of knee-jerk, and reflex iridoplegia—warrants a diagnosis of early tabes; and this is all the more certain if there be added the history or presence of ocular paralysis, difficulties of micturition, or some of the anomalous symptoms which I shall presently describe.

The *second stage* of tabes is characterised by the appearance and the progressive increase of ataxia, generally also by defects of sensation. By ataxia or inco-ordination we understand a want of harmony or co-operation in muscular contractions (as distinct from loss of power to contract), whether they be employed to produce movement (motor ataxia) or to maintain a fixed position (static ataxia); so that from the ill-combined muscular contractions actions result which are disorderly and inappropriate to their purpose. Inco-ordination, as distinguished from paralysis, has been recognised ever since Todd's and Duchenne's writings as a special mark of tabes; still, we must remember that a certain amount of loss of power often coexists with it. Inco-ordination first reveals itself in walking and standing, actions which require the co-operation of many muscles both of the trunk and lower limbs. It begins as a mere unsteadiness in walking, which is most noticeable when the patient rises to walk, or when he turns; or it may be brought out by making him march, halt, or turn to command, walk along a given line, walk backwards, walk up and down stairs, and so forth. Above all, it is worse when he closes his eyes; and often he will volunteer the statement that he cannot walk in the dark. At first the gait suggests a mere loss of equilibrium,

such as might be due to an affection of the trunk muscles; but in time the movements of the legs themselves become peculiar, the patient gets the feet crossed as he turns, and he plants them widely apart and uncertainly, looking to see where they are going. Finally, he manifests the typical "ataxic gait"; he rises from his seat and starts carefully, probably invoking the support of sticks or of a friend; he bends forward at the hips, looking at his feet; he lifts the advancing foot too high, throws it outward with a jerky movement, and brings it down again, heel first, with a stamp. This action of the lower limbs has been compared to the walk of a cock, or the movement of the legs of a marionette. Even when sitting he is unable to direct well the movements of his legs if he be told to describe a circle with his toe, touch one knee with the opposite heel, and so on. In standing, as in walking, he needs a wide basis for support, hence he is unsteady when his feet are put close together; or even supposing he can stand so, yet on closing his eyes he begins to sway and stagger. This staggering when the eyes are shut is known as Romberg's sign, and is usually considered an early indication of ataxia. Later the patient finds difficulty in standing at all without support. The inco-ordination spreads in time to the upper limbs. Here it causes an awkwardness and want of precision in the movements of the hands, so that there is difficulty in writing, in buttoning the clothes, in playing a musical instrument, in carrying out the finer manipulations of trade, and so on. If the patient be told to pick up a pin from the table, the hand wavers, and hovers over it before arriving at it, and the fingers fumble before grasping it. In the upper, as in the lower limbs, the mal-direction of movement is much increased when the aid of sight is denied. Thus, a favourite test is to tell the patient to touch the tip of his nose quickly with one forefinger, first with his eyes open (which he will do unless the ataxia is pronounced), next with the eyes closed (when the finger will probably go wrong).

Defects of sensation are usually found by the time that inco-ordination is well established. The commonest and most obvious of these begin in the lower limbs. The patient has sensations of tingling, pins and needles, numbness and deadness, and when walking may experience a peculiar feeling as if he were treading on cotton-wool or on a thick carpet. In the trunk, too, the well-known "girdle pain" may appear—that is, the sensation of a cord tied tightly round the body. Examination may then shew anaesthesia of various degrees, of various distribution, and affecting variously the several forms of sensation (touch, pain, temperature, etc.). To these points we shall recur presently, but it may be stated here that analgesia (as tested by the prick of a pin) and delay in the transmission of such sensation of pain is particularly common. Sometimes the sense of posture is lost, so that the patient cannot tell how his legs are placed without looking at them, nor imitate the position of one limb with the other when the eyes are closed. Sometimes he is unable to discriminate the difference of weights placed in his hands.

The general tendency of the ataxia is to get slowly worse, and to

spread upwards to the hands and arms. The same may, perhaps, be said of the more definite forms of sensory defect. The lightning pains in some cases disappear as the disease advances; the pupil sign and the absence of knee-jerk remain, as a rule, unaltered.

The *third stage* is but an aggravation of the second, in which the increase and spread of the ataxia has rendered the patient quite helpless. There is likely to be more definite paralysis of the bladder than before, and sexual impotency, if this have not existed from an earlier stage. Confined to bed or to a chair, emaciated and feeble, the patient's life is obnoxious to peril from bed-sores, cystitis, or intercurrent disease.

Having now described what is usually considered the standard form of tabes, I will next consider in more detail the motor, sensory, and reflex abnormalities which occur in this disease; and particularly those affections of the special senses, of the viscera, and of the joints, which often form such striking and dominant features of it as to throw the classical locomotor ataxia quite into the shade.

*Motor Affections.*—I have already alluded to two motor affections other than ataxia: first, a disproportionate fatigue after exercise, which is an early symptom in some cases, and which, according to Pitres, may occur in paroxysms just like the pains; secondly, a true muscular weakness of the legs, appearing alongside of the inco-ordination. Such weakness is in most cases a subsidiary affection, requiring examination to detect it. But it is more important to notice the many forms of genuine motor paralysis which may present themselves; and these, from their very variety, it is difficult to classify in an exact and useful manner. First, let me say that some of them may occur early in the disease, are limited in their area, and transient in nature. Such is usually the character of the very common ocular paralyses; thus, in quite the early stages of tabes one third nerve or a branch of it, one sixth, or one superior oblique, may be paralysed partially or totally, and may recover again in a few months, weeks, or even days. But even these ocular palsies may be bilateral; thus, double ptosis has been frequently noted, and paralysis of both sixths sometimes; nor do they invariably recover. Less commonly the early paralysis takes the form of a paraplegia or hemiplegia, so that a patient may suddenly lose power in both legs, or in the limbs on one side, and recover; but the recovery is followed by the symptoms of tabes. Such early transient palsies are alleged by some authors to be genuinely syphilitic, and, indeed, gummas and arterial disease have sometimes been found after death; still it must be remembered that similar palsies occur in the early stages of disseminated sclerosis, a disease with which syphilis has nothing to do. While speaking of hemiplegia two other points may be noted: first, that tabes may be heralded or accompanied by sundry other cerebral phenomena, such as fits, either epileptic or epileptiform, or attacks of vertigo or coma, recalling the much more common occurrences of this kind in the allied disease general paralysis of the insane; secondly, that, apart from the early and recoverable hemiplegia,



hemiplegia of a more permanent character, and depending probably on ordinary vascular lesions, may occur in any stage of tabes. But to return to palsies limited to the distribution of nerve-trunks; these may occur, though less commonly, in districts other than the ocular; particularly in that of the peroneal nerve, or in that of the ulnar, radial, or spinal accessory. These nerve palsies may be either single or bilateral. Bilateral laryngeal paralysis I shall discuss later. Paralysis in the district of the hypoglossal is marked by atrophy of one-half of the tongue; the affected lateral half of this organ is flabby, furrowed longitudinally, and wasted; when protruded the tip points to the paralysed side, and the paralysed muscle cannot be felt to contract; nevertheless, the patient finds singularly little inconvenience either in speaking or swallowing. It would seem that such lingual hemiatrophy is due to disease sometimes of the nerve, sometimes of the nucleus. The mention of nuclear disease brings us to yet another class of palsies of a more generalised and progressive nature than those we have been considering, clinically resembling progressive muscular atrophy, and like it caused either by multiple neuritis or by disease of spinal and bulbar nuclei. Such progressive disease may begin with wasting of the intrinsic muscles of the hands, and spread thence to the shoulder and other muscles; or in the lower limbs; or it may begin in the tongue and lips taking the form of a progressive bulbar paralysis; or in the muscles of the eyeball as a progressive ophthalmoplegia. This combination of tabes with progressive muscular atrophy is not, however, common (*vide* p. 709). Hypotonia of the muscles is an interesting phenomenon. This expression means that the muscles, albeit not wasted, perhaps not even flabby, can be stretched to a degree which in a normal person is impossible owing to the pain and the counteracting contraction set up in the muscle. Slight degrees of hypotonia are common, but may need careful examination for detection: advanced hypotonia may render possible various quaint situations. Thus, when the appropriate muscles are highly hypotonic, the thigh with the knee extended can be flexed well beyond a right angle, the patient can sit on the floor with extended legs and put his head between his knees, or can put his feet behind his head, and so forth.

*Sensory Affections.*—Sensory paralyses are extremely common. In an early case there may be none, but as the case progresses, sensory impairment of one kind or another almost always appears. Cutaneous sensation may be deficient in relation either to tactile, painful, or thermal stimuli. All forms may be affected together, but if the sensory paralysis be of the “dissociated” type, that is, if one form exist without the others, we shall probably find that the analgesia predominates over the tactile anaesthesia. Predominant paralysis of the thermal sense, which is so striking a feature of syringomyelia, is not, I think, usual in tabes. Not unfrequently the analgesia takes the form of delay in transmission of the impulse; so that if the patient’s leg be pricked, a few seconds elapse before he feels the pain. Or there may be defective power of localisation; he feels the touch or prick, but cannot tell where it is. The degree

of these cutaneous sensory paralyses may vary; in many cases there is a blunting (hypæsthesia) rather than a complete absence of sensory power. Their distribution I have been able to study in many careful charts, made by successive resident medical officers at the National Hospital, Queen Square, upon which the following remarks are based. The cutaneous anaesthesia does not always begin in the lower limbs; it is quite as common to find it limited to the upper limbs or the trunk. In the lower limbs it is sometimes difficult to demonstrate that the anaesthesia corresponds to the areas supplied by nerve-roots, since it frequently covers the whole limb; but in the trunk it is common to find a broad band of anaesthesia, encircling the body as do the dorsal nerve-root districts, and in the upper limbs a very typical distribution is along the ulnar aspect of the forearm and inner aspect of the arm, in the district of the first and second dorsal roots. Such anaesthesia is in most cases bilateral. Anaesthesia, particularly in the form of analgesia, may occur on the face, sometimes in patches, sometimes in the form of a mask, when the analgesia involves the whole face, except zones round the eyes, nostrils, and mouth. In a few cases there is analgesia of the whole surface of the body. The *deeper parts* may also be anaesthetic. Thus, there may be absence of the sense of vibration (pallæsthesia) when a large tuning-fork is applied to a bone; the testicle may be insensitive to pain when compressed; and the sense of local pain normally felt when the ulnar nerve is struck or roughly compressed (apart from the tingling in the fingers) may be absent. It is important to notice the loss of sensation in the muscles; analgesia of the muscles is common; pinching of the calves or severe pressure (for the measurement of which a special instrument has been constructed) may not give rise to pain. The tetanic contraction produced by faradism may no longer be felt (Ferrier, Golla). Further, the sense of position of the limbs, or of passive movement, may be lost. Such loss may be limited and slight, the patient cannot tell perhaps when his toe is being moved passively, nor in what position it is being held, but it may be complete and extensive, so that he cannot tell how his legs are placed unless he looks at them. It may perhaps be added that in tabes, in which the anaesthesia is due to intraspinal disease rather than to disease of the peripheral nerves, the distinction drawn by Dr. Head between protopathic and epicritic sensation does not hold good.

*Affections of Reflex Actions.*—The cutaneous reflexes are comparatively unimportant in tabes. It has been stated that the cremasteric reflex is absent when the patient is impotent. The plantar reflex is flexor in type. The presence of an extensor response would indicate that to the posterior sclerosis there had been added a sclerosis of the pyramidal tract, which in ordinary tabes is certainly very rare. In many cases of tabes, however, the movements produced on tickling the sole are rather wild and irregular, so that it may be difficult to say at first whether the reflex is flexor or not. Of the organic reflexes, difficulties of micturition, such as slowness and straining, or imperfect control over the bladder, are (as I

have said) frequent in the early stages; paralysis of the bladder may occur later, but is not perhaps so frequent as might have been anticipated. Defecation is less frequently affected. The sexual function in the man is prone at first to abnormal irritation; Trousseau states that a patient with early tabes may be capable of repeating the sexual act several times in a single night. Impotence with absence of desire supervenes sooner or later. Women with tabes have been known to bear children; but it is certainly more common to find a history of sterility, whether this be due to the tabes or to the conditions which lead up to it.

The very great importance of the tendon-reflexes in diagnosis I have already pointed out. The early disappearance of the knee-jerk is due to the fact that the spinal degeneration, attacking the fibres of the posterior roots soon after their entry into the cord, usually begins in the lower dorsal and lumbar regions, and thus cuts the reflex arcs which pass through this part. In those rare cases in which the degeneration begins higher up in the cord (cervical tabes) the knee-jerk may be retained. The disappearance of it is therefore a sign of local disease; namely, of a lesion in the postero-external column of the dorso-lumbar region. If this part be completely destroyed the knee-jerk will be completely absent, whatever the other conditions may be; but if the destruction be incomplete, it is possible that the knee-jerk may be maintained, or even exaggerated if there be simultaneous degeneration of the lateral columns. This may be seen in cases of combined postero-lateral sclerosis; and similarly, in some cases in which hemiplegia has occurred in the course of tabes, the knee-jerk of the paralysed side has been temporarily restored by the descending lateral sclerosis which results from the cerebral lesion. On the other hand, when the posterior sclerosis is advanced we may witness in such hemiplegic cases the curious combination of post-hemiplegic rigidity with absence of knee-jerk.

*Affections of Special Senses.*—Among affections of the special senses loss of smell or taste and subjective sensations of smell or taste have been described; but they are certainly infrequent. Auditory affections occur oftener—either vertigo or, what is more common, deafness; such deafness is, I believe, generally incomplete and bilateral; and its cause may be difficult to determine. In one well-known case, indeed, there was absolute deafness, and after death atrophy of the auditory nerves was demonstrated, quite analogous to the better known optic atrophy. But it would be a mistake to suppose that deafness is always due to atrophic changes in the nerve. Sometimes, certainly, the cause lies mainly in the middle ear; for inspection shews an opaque hillocky retracted membrane, indicating a fibrosis of the tympanum; in other cases examination with the tuning-fork points either to “central” mischief (which of course may be either in the labyrinth or in the nerve), or to a mixture of central and middle-ear mischief. It has been supposed that chronic fibrosis of the middle (and inner?) ear in tabes depends on some perverted trophic influence in connexion with the fifth nerve; but obviously a certain



allowance must be made for mere coincidence, since chronic middle-ear catarrh is in itself a common affection.

Affections of the eye are far more important, and foremost among these stands atrophy of the optic nerve. The frequency of this has been estimated at 15 per cent or thereabouts. It generally begins at an early stage of the tabes, preceding the ataxia, nay, sometimes preceding the pains, so that such cases may come first under the care of the ophthalmic surgeon. The patient notices a failure of vision, first in one eye and, after a variable interval, in the other; and this as a rule progresses to complete or nearly complete blindness in both eyes. Commonly, as his visual acuity diminishes, the patient becomes colour-blind, and his fields of vision become contracted, either concentrically or irregularly. Sometimes large sectors of the field disappear, and this may even produce hemianopsia. Central scotoma appears to be very rare. The defects in the two eyes, though they may differ as to their stage of degeneration, have a general symmetry both in their distribution and their progress. Visible changes in the disc begin to appear by the time that loss of vision is complained of, and sometimes even in the eye which is not known to be failing. The changes mainly consist in pallor, grey discoloration, opacity, and undue sharpness of outline. As the vascularity of the disc diminishes, as its medullated nerve-fibres atrophy, and as its interstitial tissue increases in amount, so it loses its rosy translucent aspect, and becomes pale and opaque, taking on usually a dead-grey colour, or sometimes a yellowish tint, or even a chalky-white. The physiological cup may appear deep, with undue exposure of the lamina cribrosa, or it may be filled up, so that the surface of the disc looks flattened. The edge of the disc is sharp and clear-cut all round, so that it contrasts with the surrounding fundus. The retinal vessels may remain of normal size. Upon the great prognostic importance of optic atrophy, involving as it does the prospect of utter blindness, it is unnecessary to insist. The gloomy outlook is somewhat relieved by a belief, which is commonly entertained, that when tabes begins with optic atrophy the ataxic symptoms are likely to be less marked and less progressive than usual. Neither must we forget its diagnostic importance as an early sign of tabes; for primary progressive optic atrophy is comparatively common in this disease and rare as an isolated occurrence; therefore, when a patient consults us for this alone, a careful search must be made for other symptoms.

The principal abnormalities of the pupil and the very common palsies of the external ocular muscles have already been mentioned. Less common and more serious is a progressive ophthalmoplegia externa. One after another the ocular movements become limited and abolished, till both eyeballs are reduced to permanent immobility. This condition usually comes on early in the disease, and does not pass off. It is due to disease of the oculomotor nuclei, and may be associated with muscular atrophy in the limbs. While such ophthalmoplegia is progressing, the movements of the eyeballs may be jerky and irregular; but a well-marked nystagmus, such as is so common in disseminated sclerosis, is very rare in tabes.

We now come to the subjects of visceral disturbances and of trophic lesions. Many of these form extremely striking phenomena, which, although fairly common, have little apparent connexion with spinal disease. Hence, when they manifest themselves early in the course of tabes (as they often do), and apparently as isolated facts, their true signification is apt to be overlooked.

*Visceral Crises.*—The so-called “visceral crises” must necessarily arrest attention. These consist in a sudden and violent disturbance of function, for which no sufficient external cause can be found, followed by an equally rapid return to normal, and a recurrence of the attack after a variable interval. This paroxysmal character of the “crisis” suggests an analogy to the bouts of pain, and, indeed, a typical crisis is accompanied with pains. The commonest is the “gastric crisis.” In this the pains concentrate themselves upon the epigastrium, nausea sets in, and soon vomiting too of a most severe and intractable character; the patient brings up first his food, then bile-stained mucus or clear fluid. Yet the tongue is clean, and, though the pulse may be frequent, the temperature remains normal. Severe gastric crises may be accompanied by much nervous depression, or even by collapse. After a variable time, usually one or more days, the vomiting ceases as suddenly as it began, leaving the patient well except for exhaustion. But the attack will recur, either at irregular intervals or in some cases with remarkable periodicity. In some attacks there is no pain, only the paroxysmal and causeless vomiting. Usually the gastric crises occur early in the disease, and pass off as it progresses; and later the patient, seeing no connexion between them and the paralysis which has since overtaken him, may not speak of them to the physician, or may merely mention that he is subject to “bilious attacks.” Conversely, at the time of their occurrence they may form his sole complaint, so that in any case exhibiting causeless and recurrent vomiting the possibility of an early tabes should be remembered. These recurrent attacks of vomiting and pain have been mistaken for intestinal obstruction and for appendicitis.

Analogous to gastric crises, and sometimes associated with them, are the intestinal crises, consisting of paroxysmal attacks of diarrhoea with or without abdominal pains. Sometimes the patient has attacks of tenesmus, pain, or other disagreeable sensations in the rectum. Similar pains and difficulties may arise in the region of the kidney, urethra, and bladder, so as to raise the suspicion of a calculus. In the sexual sphere men may be troubled with causeless erections and emissions, and women with erotic sensations which have been termed clitoridean crises. Anomalies of secretion may accompany, or may constitute these visceral crises. Thus, during a gastric crisis the secretion of gastric juice is stated to be increased, and the chlorine of the urine correspondingly diminished; and in the intestinal crisis there is a watery secretion from the bowel. Paroxysmal fluxes of urine, of saliva, of tears, paroxysmal sweatings, and even attacks of glycosuria have been observed.

*Affections of the Larynx.*—Affections of the larynx occur; the com-

monest of which is a bilateral paralysis, involving the abductor muscles only. The power of dilating the glottis is gradually lost; first of all, the cords, which during inspiration should diverge widely, diverge imperfectly or remain immobile during this act, though during phonation they still approximate properly; next they take up permanently a position nearer and nearer to the middle line, till the glottis is reduced to a mere chink. The symptoms of this paralysis are in its earlier stages almost nil; for the voice is unaffected (the tensors and adductors acting normally), and the only difficulty experienced by the patient is in getting breath quickly after prolonged expiratory efforts, as in speaking or singing; but in time there arises a certain stridor during respiration, evident either in the pauses of his conversation, or as a snoring noise when he sleeps; finally, as the glottis becomes extremely narrow, he finds himself liable to attacks of severe dyspnoea on the occasion of any slight laryngeal catarrh, or on extra respiratory exertion, inhalation of cold air, or other source of irritation to the larynx. Probably many of the attacks which are called "laryngeal crises" are really mere exacerbations of a pre-existing abductor palsy; but it would appear that paroxysmal attacks of cough and dyspnoea, analogous to the gastric crises, may occur without other basis than increased reflex excitability or spasm pure and simple. In some instances such laryngeal crisis is accompanied by coma and convulsions, suggesting the possibility of dangerous cerebral complications; this has been called the "laryngeal ictus." A patient with severe abductor palsy is evidently in constant danger, and a tracheotomy, if not performed as a prophylactic, may be required at any moment; yet it is surprising how little inconvenience some patients may experience even when the glottis is considerably narrowed.

Other laryngeal phenomena are unilateral paralysis, affecting movements both of abduction and adduction of one vocal cord (as in ordinary paralysis of the recurrent laryngeal trunk), which, according to Marie, is often associated with paralysis of the soft palate and hemiatrophy of the tongue on the same side; and ataxia of the larynx, an extremely rare condition, in which the cords move, but without proper rhythm or regularity, and there are sudden changes in the pitch of the voice. In some cases difficulties of deglutition occur which may be put down to abnormal innervation of the pharyngeal muscles, and are called "pharyngeal crises."

*Circulatory System.*—Frequency of the pulse was noticed by the early writers on tabes as a common symptom; less notice has been taken of this lately, possibly because the sympathetic nerve is no longer thought to be concerned in the pathology of the disease. Paroxysmal arteriospasm with high blood-pressure may accompany gastric crises (Barker). Attacks simulating angina pectoris sometimes occur and have been classed as "cardiac crises." Organic valvular disease, particularly of the aortic valves, is comparatively common; and elaborate hypotheses have been advanced to account for this; but it is probable that in some cases (looking to the age and sex of the patients) such aortic disease is a pure



coincidence, and that in others the tabes and the cardiac lesion have a common cause, namely, syphilis (*vide* also Vol. VI. p. 475). Lastly, the symptoms of Graves' disease have sometimes been observed to coexist with those of tabes.

*Trophic Lesions.*—Of trophic lesions the joint disease is the most remarkable. As the characters of this were laid down by Charcot, it has been named Charcot's disease. It has been fully described on p. 98.

Closely allied, no doubt, to the phenomena of the joint disease is that of *spontaneous fracture of bone*, which has been described on p. 96.

By a similar combination of bone and joint disease may be produced a peculiar distortion of the foot; first, a firm, painless swelling forms upon the dorsum, subsequently the inner border becomes thickened, the arch is flattened, and the whole foot shortened and deformed. This condition differs from the club-foot described by Joffroy, which is a kind of equinovarus with flexion of the toes, produced (it would appear) partly by a neuritis which has caused muscular palsy and atrophy, partly by pressure of the bed-clothes upon the flaccid and paralysed feet (*vide* p. 102).

Another affection of the lower limbs, possibly trophic, which has been seen in some cases of tabes, is rupture of the tendo Achillis.

Perforating ulcer of the foot is not very uncommon, and is often quite an early symptom. This begins as a corn, seated commonly, though not invariably, on the ball of the great or little toe; beneath this, or in the centre of it, suppuration takes place, so that an ulcer or sinus is formed, which in bad cases may extend right into the joint beneath. It is common to find some anaesthesia in the neighbourhood of such an ulcer. Gangrene of the toe occasionally supervenes, and either for this cause or on account of the inconvenience entailed by the presence of an intractable sore, amputation may be required. Nevertheless, the less severe forms of perforating ulcer, which are also the commonest, often heal by themselves, or under very simple remedies (*vide* p. 93).

Deformities and loss of the nails, chiefly of the big and little toes, have been seen in tabes, and have been associated with the nervous disease on account of the prevalence of pain or of anaesthesia in the parts concerned. The teeth in some cases have been observed to drop out; and even large pieces of the jaw-bone to come away, painlessly.

As to cutaneous affections, herpes sometimes occurs, preceded by lightning pains in the district of the eruption; sometimes also crops of small subcutaneous ecchymoses, also preceded by pains; sometimes, again, widespread effusions of blood under the skin. Subcutaneous oedema may occur in connexion with the joint disease, and possibly alone.

*Mental Affections.*—In most cases the mind is not affected. Various psychical troubles, particularly in relation to the early stage of the disease, have been described by Fournier, but these are hardly a matter of general experience. Other authors have thought that the contented and hopeful way in which many patients bear their terrible disease is in itself an evidence of some mental alteration. The opposite bias, namely,

towards undue despondency and hypochondriasis, though less common is far from unknown. But it is of importance to remember that in the course of tabes symptoms of general paralysis of the insane may supervene; this is hardly surprising when we remember the very close relations between the two diseases. Both occur in syphilised subjects, and in men rather than women. In general paralysis there may exist, over and above the cerebral lesion, a systemic spinal sclerosis, sometimes predominating in the posterior columns; and in such a case the patient may be ataxic, and present the reflex iridoplegia and the absence of knee-jerk which are characteristic of tabes. So that it has been asserted that the two diseases are essentially the same, and that general paralysis is a "tabes of the brain." However this may be, in ordinary tabes mental symptoms are usually absent, yet sometimes they do supervene in the form of exaltation, excitement, and the grand delusions characteristic of general paralysis. With the onset of such a mental state the walking powers may appear to improve. The prognosis is, no doubt, very grave, still the mania does in some instances pass away and leave the patient in his previous state; more commonly, however, he gets rapidly worse both in mind and body, and dies a helpless and emaciated general paralytic.

**Course of the Disease.**—The ordinary course of tabes consists in a slow but steady progress, the powers of locomotion growing worse by degrees, and the inco-ordination spreading to the upper limbs. The several stages are to be measured by years, or at any rate by many months. Not infrequently, however, a natural arrest appears to take place; for patients may suffer pains for many years without becoming ataxic; and others already ataxic may be seen going about for an indefinite time. Many symptoms, such as the early palsies, the pains, and the visceral crises, may disappear as the disease advances; but thoroughly established ataxia rarely, if ever, disappears completely, though instances of improvement may be quoted. Neither does the knee-jerk return when once completely abolished, nor the pupil regain its normal contractility. It is, indeed, obvious that when the fibres of the posterior roots and columns are destroyed they are never likely to be replaced; nor is it easy to see how their functions can be undertaken by other parts, and therefore such symptoms as depend on this lesion will persist. Still many symptoms may be caused in other ways, and particularly by peripheral nerve disease, and then may be far less hopeless. On the whole we may say that, the more typical and steady the march of the disease, the less the chances of improvement in the particular case.

Tabes does not necessarily shorten life, and doubtless many patients outlive their physicians; but danger may be anticipated in particular cases from laryngeal, cardiac, or cerebral complications; or in the later stages from bed-sores or bladder troubles, or (which is still more likely) from intercurrent disease. It is unusual for tabes to run a rapid course; still patients have been known to become ataxic in a few weeks or months, or even, it has been said, in a single night.

There are cases in which the pains, anaesthesia, and ataxia affect the upper limbs first; or in which symptoms first appear in the districts of the cranial nerves. In these (which have been called "cervical" or "cerebral" tabes respectively) the sclerosis presumably begins in the upper parts of the cerebrospinal axis, not as usual in the lower. The diagnosis then may be far from easy, especially in view of the fact that the knee-jerk is likely to remain unaffected longer.

It is important to remember that many of the anomalous symptoms which I have described may occur quite early in the disease; this applies particularly to the optic atrophy, the visceral crises, the joint disease, perforating ulcers of the feet, and abductor paralysis in the larynx.

**General Considerations.**—As we have now described the pathology, symptoms, and course of tabes, I propose, before turning to diagnosis and treatment, to make some general remarks on the disease. The study of tabes has been facilitated by the fact, that both during life and after death we can generally arrive at a tolerably definite diagnosis. For though its manifestations may be very varied, yet there is nearly always a substratum of certain cardinal symptoms; and anatomically it presents a very definite lesion, namely, symmetrical degeneration of certain portions of the posterior columns, and of the posterior-nerve roots. This degeneration is in a double sense progressive: first, in the neuron itself, where it spreads from the terminal twigs along the nerve-fibre to the cell-body, till the nerve-tissue perishes and is eventually replaced by neuroglial overgrowth; secondly, because it does not remain limited to one set of nerve-roots and their distribution, but tends to attack, in upward series, the roots of many levels. But although the characteristic lesion, without which we could hardly reckon a given case as tabes, be degeneration of the posterior columns, it is likely that the morbid process has a wider incidence. This is rendered probable by the variety and extent of the symptoms, and is corroborated anatomically by the facts of optic atrophy and of peripheral nerve degeneration in tabes. Tabes from this point of view has been called a "great sensory neurosis": that is, a disease which selects for attack the afferent nervous apparatus, whether central or peripheral. As such it may be contrasted with amyotrophic lateral sclerosis, a disease which falls specially on the efferent part of the nervous system. Still, it is not entirely confined to afferent structures, as is shewn by the frequent occurrence of motor paralysis, and by the facts that degeneration has been demonstrated in motor nuclei and motor nerves also. Such a widely spread process suggests a constitutional cause, and this consideration leads us to doubt the hypotheses which attribute the origin of tabes to purely local lesions, such as syphilitic meningitis, syphilitis arteritis, trauma, and the like. The view adopted above, namely, that some antecedent disease, like syphilis, has impaired the vitality of certain neurons, and so set up premature decay in them, covers the facts better, but is obviously difficult to prove directly.

Doubtless the symptoms of tabes, varied though they are, are capable



of being referred to their anatomical basis, but it is difficult, in the present state of our knowledge, to do this for all of them. Todd, who first described the symptoms of inco-ordination, connected it with disease of the posterior columns; and in tabes we think there can be little doubt that this connexion holds. We may at least say that the ataxia is due to blocking of afferent impulses from the periphery. But there are difficulties in following out this statement into detail. First, what is meant by ataxia? In quite an early stage the ataxia of tabes may consist in a mere unsteadiness of gait, not easily distinguishable from a slight degree of cerebellar ataxia. It is tempting to suppose that this may be caused by the degeneration of the fibrils which ramify around the cells of Clarke's column, whereby the connexion between the posterior-root system and the cerebellum is cut off. Romberg's symptom has been explained by Dr. Mott on the same basis. But in more advanced tabes the ataxia is not merely a disturbance of equilibrium, but a disorganisation of the movements of the limbs. For the cause of this we must look further; probably to the degeneration which blocks the connexions between the posterior roots and ( $\alpha$ ) the cerebrum (columns of Goll) or ( $\beta$ ) the anterior horns of the cord (short fibres, see p. 738), since by one or both of these routes afferent impulses ascend from the periphery, which guide the motor centres and enable them to provide that harmony of muscular contraction which is necessary for movement. But what kind of afferent impulses are most important for this purpose? One would naturally think those which come from the muscles, joints, and tendons, and which convey the sense of position. And it has been stated as a fact (though all authorities do not agree to the statement) that ataxia is always accompanied by some loss of sense of position. It is certain, at any rate, that a patient may be ataxic without any loss of tactile sensation. We therefore think that of the ingoing impulses those from the deeper structures, such as muscles and joints, are most important, those from the skin subsidiary. Another possible factor contributing to the ataxia of tabes must be mentioned, namely, the muscular hypotonia (see p. 752). This loss of tone, which may reasonably be ascribed to the degeneration of the short fibres which link up the posterior roots with the anterior horns (p. 738), may affect co-ordination of movement as follows:—The volitional contraction, in a given movement, of the muscles which are the prime movers, should be moderated and controlled by the reflex tonic contraction of their antagonists; but where this moderating influence is absent, the movement is likely to be irregular and jerky, as is the case in advanced tabes.

The lightning pains are commonly attributed to irritation of centripetal nerve-fibres within the cord (namely, the "*bandelettes externes*," which Pierret has shewn to suffer early in the disease); but it is possible that in some cases peripheral neuritis may also contribute to the production of pains.

The loss of knee-jerk Westphal refers to degeneration of the posterior-root fibres in the dorso-lumbar region, just after their entry into the cord.

It is obvious that any rupture of the reflex arc between the posterior roots would explain this symptom, as well as the loss of muscular tonus.

J. Ross considered that the reflex iridoplegia is due to disease of fibres connecting the anterior corpora quadrigemina with the nuclei of the third nerves; but this view has not been universally accepted. Dr. Ferrier leans to the view that it is due to disease of the ciliary ganglion.

The explanation of many of the accessory symptoms (visceral, trophic, etc.) is still uncertain. Dr. T. Buzzard, observing that gastric crises and joint disease frequently occur in the same patient, suggests that both may be due to some lesion in the neighbourhood of the vagal nucleus, where may be placed centres which control the functions of the stomach and preside over the nutrition of the bones and joints. Another explanation of symptoms of this class is, that they depend on peripheral neuritis, and that the occurrence of several such symptoms in the same patient may indicate a form of the disease in which the peripheral nerves are specially prone to suffer. A third explanation might be hazarded that they are due to faults in the connexions between the posterior-root system and the cells of the intermedio-lateral tract (p. 738). But all these explanations are at present merely speculative.

The diagnosis may often be made before ataxia sets in; and a well-established case of ordinary tabes is certainly not easily mistaken, except it be for certain cases of peripheral neuritis. Most cases of *peripheral neuritis* exhibit, it is true, paralysis rather than ataxia, accompanied usually with some muscular wasting and changes in electrical reaction; and such features form a sufficient contrast to ordinary tabes. But sometimes peripheral neuritis produces ataxia without distinct paralysis, and since there may be pains and sensory defects, and since the knee-jerks may disappear, much difficulty of diagnosis may arise. Yet a diagnosis must be made if possible, for the chances of recovery are far greater in neuritis than in tabes. The points most useful for this purpose are as follows:—For peripheral neuritis it is usual to find some immediate cause; either some toxic agent such as alcohol, lead, or arsenic, some antecedent fever, particularly diphtheria, or some constitutional affection like diabetes; for tabes this is not the rule. Peripheral neuritis increases with comparative rapidity, so that the ataxic stage is reached probably in a few weeks or months, and the affection may spread quickly to the arms; in tabes there is a long preliminary stage, and the upper limbs may escape long after the walking powers have been impaired. Accessory symptoms, such as visceral and trophic disturbances, are far more common in tabes. Lastly, the state of the pupil is of extreme importance. Where there is distinct and definite iridoplegia we may generally diagnose tabes; but when the pupil reacts normally, or is fixed, reacting neither to light nor to accommodation, the diagnosis in default of other evidence must remain doubtful. Here, as in other doubtful cases, the investigation of the cerebrospinal fluid (see p. 746) may be of much value. Another distinction between the two diseases, which is easy to investigate, is that in peripheral

neuritis the muscles are often tender to pressure, whereas in tabes they are often insensitive to it (*vide* p. 458).

The diagnosis from *general paralysis* is equally important, for here the prognosis (at least *quoad vitam*) is worse than in tabes. Between the general paralysis that begins with characteristic mental symptoms and ordinary tabes there can be little risk of confusion. But there may be a spinal type of general paralysis, in which the patient exhibits ataxia, loss of knee-jerk, reflex iridoplegia, and perhaps other symptoms which we have described as belonging to tabes. We must then look carefully for signs of mental degeneration, such as early loss of memory, irritability, hebetude, and business incapacity (which I believe to be exceptional in pure tabes), and particularly for the incipient affection of speech, and tremulousness of tongue, lips, or hands, which characterise general paralysis. In general paralysis the progress of the disease is commonly more rapid than in tabes, just as we expect its conclusion to be. Absence of lightning pains, from which most patients with tabes suffer at some time, should also suggest the possibility of general paralysis.

The name of "*ataxic paraplegia*" has been given to cases in which the lateral as well as the posterior columns are degenerated, and indicates the leading clinical fact, namely, that here paralysis of the legs, usually of a spastic type, is associated with ataxy. The most definite type of this disease is subacute combined degeneration (*vide* p. 786). There is little risk of confusing this with tabes, except it be in the late stage, when the knee-jerks have disappeared. Even then, however, the plantar reflex remains (as it has been throughout the disease) of the extensor type, which is not the case in tabes (*vide* also p. 802).

Ataxia from *cerebellar disease* is characterised by a staggering, tipsy gait, often with a tendency to fall to one particular side; jactation of the feet, like that seen in advanced tabes, has been described, but certainly is not the rule. The knee-jerks, too, are occasionally absent in cerebellar disease. Here the resemblance to tabes ends, for there is neither reflex iridoplegia, nor lightning pains, nor other sensory symptoms. The same may generally be said of Friedreich's form of "hereditary ataxia"; moreover, the age at onset, the family history, the affection of speech, and sundry other data will aid us here.

An ataxic gait is sometimes seen in *disseminated sclerosis*; but the knee-jerks are usually exaggerated, the pupils act normally, and nystagmus, so rare in tabes, is common; whilst lightning pains, common in tabes, are rare (*vide* also p. 843).

In *syringomyelia* the lower limbs may be ataxic, but are more commonly paraplegic; the disease usually manifests itself first in the upper limbs and upper parts of the body; sensation is affected in a special manner, the temperature sense being first abolished; muscular atrophy, spontaneous whitlows and necroses of the phalanges, and lateral curvature of the spine are common, whereas in tabes they certainly are not.

*Hysteria* does not counterfeit tabes; for where the knee-jerk is absent, and the pupil does not react to light, hysteria may be so far excluded;



and, on the other hand, where both these signs are absent, *tuberculosis* cannot be certainly diagnosed.

**Treatment.**—Concerning treatment we are not in a position to make very definite and satisfactory statements. There are difficulties, obvious enough, in the way of estimating results ; for the progress of the disease is slow, nay, sometimes it seems to undergo natural arrest, so that long observation is necessary before we can assert that a remedy has done permanent good. Moreover, even as the disease advances, some of the most striking symptoms, such as lightning pains and gastric crises, may spontaneously disappear, whatever the treatment may have been. But in spite of such sources of fallacy we are bound to consider how suffering may best be mitigated, and arrest of the disease procured.

For the pains I consider antipyrin, and drugs of this class, to be fairly trustworthy remedies. Ten grains of antipyrin, or an equivalent of antifebrin, repeated hourly for three or four doses, will often cut short a bout of lightning pains. An excellent combination is phenacetin (or antipyrin) with citrate of caffeine and aspirin, 5 grains of each of the three drugs, to be given when the pains begin. Or, if the pains be less paroxysmal, antipyrin, or one of its congeners, may be given regularly three or four times daily. Salicylate of sodium, colchicum with alkalis and with iodide of potassium, and aluminium chloride are also drugs that may be used in cases in which the pains are a prominent feature. I have known repeated doses of castor oil relieve the pains when other medicines have failed. When the pains are very severe and intractable, subcutaneous injections of morphine must be given, but the great danger of creating a habit must be borne in mind, so that morphine should be our very last resource. Gastric crises and other paroxysmal visceral disturbances may resist all treatment. Drop doses of tincture of iodine may sometimes do good ; so may atropine ; injections of morphine, again, should be a last resource. For the urinary derangements ergot has been particularly recommended by Charcot, and belladonna is certainly useful. The urine should be carefully watched for indications of cystitis, and symptoms thereof should be met by nrotropin, and by careful surgical treatment.

Looking upon the disease as a progressive degeneration of the nerve-centres, we shall advise the patient to aim at some quiet, wholesome mode of life, free from anxieties and from the drive of excessive business ; and to abstain carefully from excess in alcohol, smoking, and sexual indulgence, if indeed he be still sexually capable. Remembering, too, that the pains are intensified by cold and damp, we shall advise him to live in some dry and healthy situation, sheltered from east winds, and to winter abroad if he can afford to do so. The general nutrition must receive careful attention—iron, cod-liver oil, and other tonics being used as required, and a wholesome nutritious diet insisted upon ; for patients with *tuberculosis* are generally pale and thin, sometimes actually wasted. Prolonged confinement to bed is not advisable, except in special cir-

cumstances ; it is better that the patient should continue to practise the use of his limbs ; but he must, on the other hand, avoid fatigue.

Of hydropathic treatment some authorities speak highly, others with reserve ; and it would seem that no vigorous or extreme measures should be attempted in this direction, nor too much expected in the way of relief.

Electricity has been employed in two ways: first, faradism, applied to the skin with the wire brush, chiefly with the view of relieving pain, of restoring sensation to anaesthetic parts, and, possibly, of acting upon the spinal cord in a reflex way ; doubtless static electricity might be used for the same ends ; secondly, galvanism applied to the spine so as to reach the cord, if possible, and to modify its nutrition, a current being used of as many milliamperes as can be borne. Two very large electrodes should be used, and placed the one over the sacrum, the other higher up. The current is gradually raised to the maximum, and the upper electrode moved slowly up and down the spine without rapid makes or breaks. It is rather doubtful how far electrical treatment can modify the general course of the disease ; but at any rate electricity may be very properly employed for the treatment of the various paralyses which occur in the course of tabes, being applied, for this purpose, to the affected nerves and muscles in the ordinary way.

As to drugs, considering the prominence assigned to syphilis as a cause, it might be thought that mercury would take the first place. On the hypothesis that tabes originates in some local syphilitic lesion, say a meningitis (see p. 744), it might be reasoned that mercury would stop the progress of the disease ; if the view expressed in this article is adopted—that tabes is a degeneration consequent on bygone syphilis, a “*damnosa haereditas*” from the past—then there is no reason for giving mercury. We have then to look at the question empirically, and from this point we think that there is no conclusive evidence in favour of mercurial treatment, and some authors think it positively harmful. Iodide of potassium, on the other hand, in small doses, certainly seems to be of benefit in some cases, probably not so much as an antisiphilitic as by some more general action. Sir W. Gowers, who thinks that much may be done by the persevering use of appropriate drugs, speaks highly of arsenic ; and, where there is much pain, of aluminium chloride. The old-fashioned treatment by nitrate of silver, administered in small doses for a long time, is capable, I believe, of doing some real and permanent good.

Various mechanical and surgical methods of treatment have been tried ; such, for instance, are the application of counter-irritants—setons, blisters, and particularly the actual cautery—to the spinal column, and stretching of one or both sciatic nerves, a practice which has rightly been discontinued. Suspension may be briefly described as follows :—a tripod and pulleys are provided similar to those used for the application of a Sayre's jacket ; to the pulleys is attached an iron cross-bar ; from the centre of this depends a leather

apparatus, into which the patient's chin and occiput are fitted, and from the ends of it hang padded straps with which to support his axillae. By the pulleys he is raised gradually off his feet, and suspended by head and arms, first for half a minute, and for longer periods on subsequent occasions till four minutes is reached. If thought advisable, he can be told to raise his arms now and then, so that he hangs by the head only. This process is repeated once a day for thirty days or more. Suspension, originally proposed by Motschutkowski, received the sanction of Charcot in France, and was introduced into this country, I believe, by Dr. De Watteville. Trustworthy observers reported favourably upon this method, but it has scarcely fulfilled its early promise, and appears to have fallen into disuse.

In none of these modes of treatment do we place much confidence; but there is a plan of treating the ataxia, which should not be neglected even in advanced cases. The principle of it is to re-educate the patient, by practice, in the orderly performance of movements. Let us suppose a patient to be unable to stand. He begins by practising the simplest possible movements of the lower limbs, such as lifting them slowly off the bed, slowly flexing and extending the knee, and then slowly replacing them. When he can do this steadily, it is usual to provide some simple apparatus, such as boards in which notches and holes are cut, and the patient, after lifting the limb, slowly brings it down with the heel in a given notch, one notch after another. When he can do the exercises with his eyes open, he next practises them with his eyes shut. Such exercises are practised, say for a quarter of an hour, two or three times daily, but always stopping short of fatigue. The transition from mere movements of the legs to standing or walking is difficult. He must be supported on each side at first; or hold on to a rail and struggle about on his own account, till he can be trusted in a "go-cart," and after that to crutches or sticks. Should the ataxia be less severe, the patient being still able to walk alone, he should, besides doing the exercises in bed, practise walking along a given line, or planting his feet in footsteps marked out on the floor. This method of treatment is capable of great elaboration and adaptation to individual cases, for details of which we must refer to the writings of Frenkel; but by the persevering use of even simple means, such as we have described, we have seen patients, who on admission to hospital were unable to stand, rendered capable of walking with very moderate support.

J. A. ORMEROD.

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J. A. O.

## FAMILIAL AND HEREDITARY ATAXIA

By GORDON M. HOLMES, M.D., M.R.C.P.

THE classification of the different varieties of familial or hereditary ataxia is difficult, as apart from the type originally described by Friedreich little is yet known of their pathology, and it is on the nature and distribution of the structural lesions underlying the symptoms that the classification of the disease must be based. Further, some cases are intermediate between the different types, and other cases are closely related to familial spastic paraplegia.

The characteristic feature, however, of the cases considered in this article is that they arise in consequence of an inherited defect in certain nerve tracts or cells and without the intervention of any extrinsic morbid agent; in Raymond's words, they result from the "premature physiological senescence of certain organic systems." The essential anatomical change is a primary degeneration of certain afferent tracts to the cerebellum, or of the cerebellum itself, though frequently the dorsal columns of the spinal cord and the pyramidal tracts are also involved. Clinically, they are characterised by inco-ordination of volitional movement, and especially a difficulty in maintaining equilibrium during

progression, and static ataxia; there is occasionally also a defect in some form of sensibility or spastic symptoms. As the disease depends on inherited defects, optic atrophy, ophthalmoplegia, and other symptoms unrelated to the cerebellum may occur, as the result of primary degeneration of other parts of the central nervous system from the same cause. The disease can often be traced through several generations of a family, but more frequently it is found in the one generation only; sporadic cases are not uncommon. The following pedigree of hereditary ataxia which has been worked out by Sanger Brown illustrates the disease through five generations of a family:—

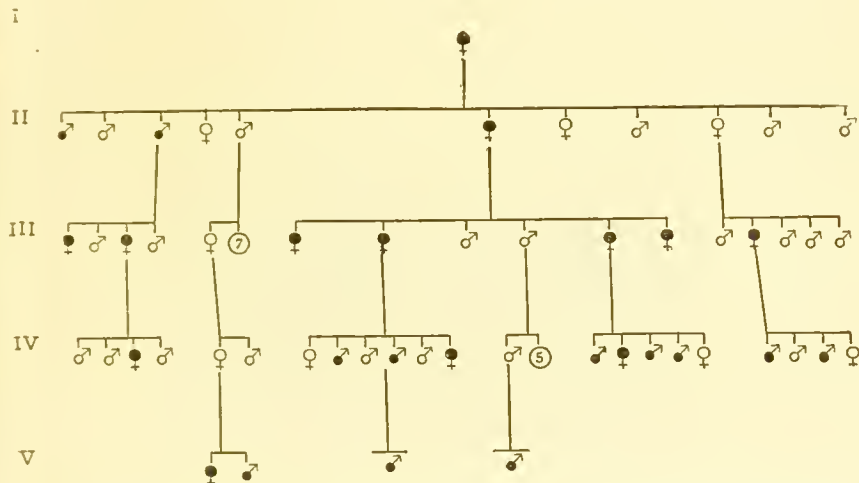


FIG. 89.—Pedigree of hereditary ataxia (Sanger Brown). ♂ = unaffected male; ● = affected male  
 ♀ = unaffected female; ● = affected female; (5) = five other unaffected children in family.

The phenomenon of *anticipation*, that is the manifestation of the disease at an earlier age in each successor, either in members of each succeeding generation as a whole or in successive children of the one parentage, which is frequently present in hereditary nervous diseases, is well illustrated in this family; in the first generation shewn in the pedigree the disease appeared at 45 years of age, in the second generation the average age at its onset was 39 years, in the third 28 years, in the fourth 22 years, and in the fifth 11 years.

Classification is, however, necessary for clinical purposes, though any adopted at present may be artificial and provisional. The type originally described by Friedreich must be retained, though, as experience has shewn, it cannot be defined as strictly as earlier authors believed. Other forms and anomalous cases, though closely related to it, are not so easily dealt with. Some years ago Marie attempted to group them together under the title *hereditary cerebellar ataxia*, "the fundamental anatomical fact on which this morbid entity was based being atrophy of the cerebellum, the spinal cord being normal or presenting lesions of no importance" (Londe); but, with the exception of Dr. Fraser's case (91), the

cerebellum has been normal in the cases originally included in this category by Marie. The title hereditary cerebellar ataxia must therefore be discarded as erroneous and inaccurate. The following classification, based on the pathology of the disease as far as it is yet known, is better suited to clinical purposes.

I. *Friedreich's disease*, a combined system-degeneration of the spinal cord.

II. *Spino-cerebellar ataxia*, dependent on a primary degeneration of the spino-cerebellar tracts, but frequently associated with degeneration of the dorsal columns.

III. *Cerebellar ataxia*, in which the morbid change is limited to the cerebellum and its immediate connexions.

I. FRIEDREICH'S DISEASE.—In 1861 the form of spinal disease which has since borne his name was originally described by Friedreich. It is characterised by a tendency to attack more than one member of the same family, though it is seldom directly hereditary and sporadic cases are not uncommon; by its onset in childhood or adolescence; and by its slowly progressive course. Its chief symptoms are inco-ordination of voluntary movement and ataxia, with little loss of muscular power. As a rule there are no sensory changes, the tendon-reflexes are abolished, the plantar response is of the extensor type (Babinski's sign), and the patient presents nystagmus, an alteration of speech essentially due to ataxia of the muscles of phonation and articulation, and skeletal deformities, especially of the spine and feet. The morbid change responsible for these symptoms is primary degeneration of the dorsal columns of the spinal cord, of the spino-cerebellar tracts, and of the pyramidal tracts. The variations in the clinical symptoms depend on the relative degree of the affection of each of these systems. Friedreich's disease, however, is by no means a constant and immutable type; almost every one of its symptoms may be absent in certain cases, and other irregular or adventitious symptoms are frequently found in association with those which are regarded as characteristic.

**Etiology.**—The characteristic primary degeneration of certain tracts of nerve-fibres in the spinal cord is generally assumed to be due to a defect in their original constitution; it sets in and as a rule remains independent of any morbid agent, extrinsic or intrinsic. The remarkably small size of the spinal cord, which is found even in patients that die young, is strong evidence of a congenital defect, a conclusion which the family nature and the occasional inheritance of the disease support.

Consanguinity of the parents has been occasionally noted, and epilepsy, insanity, and various neuroses are not uncommon in the relatives. In a remarkably large proportion of the cases, as Friedreich originally pointed out, one of the parents, especially the father, has been a chronic drunkard. Congenital syphilis is rarely a possible etiological factor, though Bouché and Bayet found the two diseases associated, and Beco and Allen Starr observed Friedreich's disease in the offspring of syphilitised



parents. In the case recorded by Philippe and Oberthür the disease appeared after syphilitic infection. The history is often to the effect that the symptoms commenced or became aggravated after an acute infective illness, but these cannot be regarded as more than exciting factors.

Bing (5) has recently attempted to apply Edinger's *Ersatz-Theorie* to this disease. According to Edinger portions of the nervous system which do not receive sufficient nutrition, or are under-developed or not normally resistant, may degenerate under the stress of relative or absolute overwork; in Friedreich's disease the spinal cord is congenitally small, and those tracts on which the chief stress of function falls, the longer afferent neurons and the pyramidal tracts, succumb to the work for which they are not fitted.

*Heredity.*—Friedreich's disease, although called hereditary ataxia, is seldom directly hereditary; on the other hand, in the great majority of the cases more than one member of the family is affected. Schoenborn



FIG. 90.—Photomicrograph of a section of the eighth cervical segment of the cord in Friedreich's disease, stained by Weigert's method. The degenerated portions appear pale.

found a family incidence in 114 of the 200 cases he analysed. Yet in a not inconsiderable number of recorded cases the same disease occurred in the ascendants or in collateral lines. Rüttimeyer, for instance, observed eight patients in four branches of a family descended from a common ancestor, from whom they had also inherited the nickname "staggerer." Biro and Peiper each saw the disease in a mother and a daughter, and Brock and Glorieux found cases in three generations of different families. It may be transmitted through either males or females. Occasionally there is not direct heredity, but the disease occurs in families in which there seems to be a proclivity to spinal disease; for instance, the mother of some of Dr. Ormerod's cases had spastic paraplegia (44).

*Sex.*—It appears that males are affected somewhat more frequently than females; of 164 cases which I have analysed, 94 were males, 70 females.

*Morbid Anatomy.*—The essential pathological alteration is a primary degeneration of the dorsal columns of the spinal cord, of the pyramidal tracts, and of the spino-cerebellar tracts. The degeneration of the dorsal columns is the earliest change and generally remains the most prominent;

the endogenous fibres are less affected than the exogenous. In the lumbosacral segments the whole column except the cornu-commissural zones and the fibres in the immediate neighbourhood of the dorsal horns degenerate, but in even the most advanced stages a certain proportion of the fibres of every region remain intact. In the upper dorsal and cervical segments Burdach's columns are, as a rule, less affected than the dorso-median columns. Lissauer's zone is usually intact, though it occasionally degenerates. A definite loss of fibre and secondary sclerosis of the dorsal roots can generally be determined, these changes becoming greater from the spinal ganglia towards the cord. Alterations in the spinal ganglia are rare or insignificant, and evidently only secondary to the degeneration of the dorsal roots. There is usually some diminution of the dorsal root-fibres and collaterals to the ventral horns, and considerable degeneration of the coarser root-fibres that terminate in Clarke's column.

The degeneration of the pyramidal tracts in the spinal cord is usually less intense than that of the dorsal columns, and apparently commences later. As in the other primary system-degenerations, it is greater in the lower than in the higher segments, and, as a rule, is not apparent above the level of the medulla oblongata. The spino-cerebellar tracts are also constantly degenerated, the direct cerebellar tract being more seriously involved than Gowers' tract; indeed the latter has been found unaltered in some characteristic cases. Clarke's columns, from which the direct cerebellar tracts take origin, are always atrophied; they contain few myelinated fibres, and their cells disappear. The neuroglial overgrowth, which follows the degeneration of these tracts, is usually much greater in the dorsal than in the lateral columns; in the dorsal columns the interstitial tissue is in such great excess and arranged in such irregular whorls or "tourbillons," that Dejerine and Letulle regarded it as the primary change.

In addition to these system-degenerations the spinal cord is usually remarkably slender, often not more than half the normal size in cross-section. This smallness, generally regarded as congenital, has been observed even in patients who died in the earlier stages of the disease.

The forebrain is unaffected and is usually fairly well developed; histological examination has revealed atrophy and disappearance of the giant cells of the ascending frontal gyrus from which the pyramidal fibres spring, but this is evidently a secondary change only (Mott, Holmes). The condition of the cerebellum has attracted much attention, as many of the symptoms of Friedreich's ataxia have been attributed to morbid changes in this part of the nervous system (Senator, Raymond). There has not, however, been any disease of the cerebellum in the great majority of the cases in which a careful necropsy has been made; indeed the cerebellum was normal in all the typical cases that were examined till 1898 (Mackay). Since then, however, pathological changes have been discovered in the cerebellum by Philippe and Oberthür, by Bing, and by Perrero, though in the latter two cases the abnormality was largely a

hypoplasia. We may therefore conclude that disease of the cerebellum is rare and does not belong to the typical anatomical picture.

Atrophic and degenerative changes have been observed in the peripheral nerves (Dejerine and Thomas, Mackay).

The clinical symptoms can be easily correlated with the anatomical lesions which characterise the disease. It is now generally agreed that the dorsal columns of the cord convey the impressions from the deeper structures of the limbs, which reach consciousness and subserve the sense of position; the interruption of these impressions, as is also seen in tabes, produces ataxia of movement. That the sense of position, as it is usually tested, is not constantly found to be absent in Friedreich's disease can probably be explained by the persistence, as shewn by stains for the medullary sheath, of a considerable number of normal fibres even in the densest sclerosis, and also of other naked axis-cylinders (Müller). The spino-cerebellar tracts, on the other hand, subserve the conduction of the afferent impulses to the cerebellum which do not reach consciousness, but underlie muscular co-ordination; the ataxia of movement and the static ataxia which do not develop parallel to the loss of the sense of position can be consequently correlated with the degeneration of these tracts. The affection of the pyramidal tracts produces weakness of volitional movement, but as their degeneration is generally late, severe parietic symptoms usually appear only in the late stages of the disease.

**Symptoms.**—The onset of the disease is invariably slow and gradual. The first symptoms generally appear between six and ten years of age, but in a considerable number of the cases the onset is delayed till the years of puberty; in a family observed by Dr. W. J. Potts, in one member of which I confirmed the diagnosis by necropsy, the symptoms did not appear in the three members affected till after thirty years of age. On the other hand, many cases have been recorded in which symptoms were present from early childhood. As a rule, the age-incidence is approximately the same in each family. But the onset is so slow and gradual that it is frequently impossible to determine exactly the age at which its symptoms began. Almost invariably the first sign is a certain awkwardness of gait, and a tendency for the child affected to stumble and fall more than he had previously done. In many cases, however, the child has never been quite strong on his legs or able to join on equal terms with other children at play. A case is recorded by Dr. Tresidder in which, though definite symptoms did not appear until the age of nineteen years, the patient had never been able to run properly or to skate. As a rule walking is not much more difficult in the dark than in daylight, though occasionally the difficulty is observed for a time only in the dark (Brock). Gait slowly becomes more irregular and more difficult, and gradually acquires that reeling and staggering character described by Charcot as "*démarche tabéto-cérébelleuse*." It may be likened to that of a drunkard; the patient walks with his feet widely separated, staggering and reeling from side to side, but not deviating far from the direct line of progression. The steps are usually short, unequal



and irregular, and the movements of each foot as it is raised from the ground are evidently poorly co-ordinated and ataxic. The leg is not, however, unduly raised, or thrown forwards or stamped to the ground so strongly as in tabes. The inco-ordination and difficulty in maintaining balance become very prominent in the act of turning, or in rising quickly from a seat. Walking becomes more and more difficult as the disease progresses, and the limbs so feeble that assistance is needed; at this stage the feet can scarcely be raised from the ground and are dragged along it. Finally, unless life is ended by an intercurrent illness, the patient is bedridden. The inco-ordination of the lower limbs is less evident in movements performed as the patient lies in bed, but it can be generally demonstrated by the usual tests.

A symptom equally prominent with the inco-ordination of volitional movement is the static ataxia which results from a defect in the co-ordination of the muscles required to maintain a fixed position against external forces; in standing the patient oscillates from side to side, and tremor of the trunk and head is almost constant. The patient has, consequently, considerable difficulty in balancing himself on his feet; in many cases this difficulty is considerably increased when his eyes are closed, but in other cases Romberg's sign is absent.

At a variable period after the legs are affected the arms are involved. At first there is only a certain awkwardness in their movements, but these gradually become more and more ataxic. This inco-ordination has special though not distinguishing characters; it resembles the ataxia due to cerebellar disease more closely than that of tabes; in attempting to grasp an object the hand hovers above it irregularly for a time and then suddenly falls on it, as a bird of prey swooping on its victim, as Charcot described it. The finer movements are usually the more severely affected. In the arms inco-ordination of movement is constantly associated in the fully developed disease, with irregular involuntary movements, which are frequently described as choreiform. As these depend on a want of harmony between the muscles that maintain the position of the limbs, they appear only when the limbs or some of their segments are unsupported. Similar irregular tremulous or nodding movement of the head, and slight swaying movements of the trunk as the patient sits unsupported, are also prominent features in the advanced stages of the disease. They can be partly controlled by volition, and become more marked on diverting the patient's attention.

The strength of the individual movements is little or not at all impaired at first, but as the disease advances the limbs gradually become weaker; the lower extremities are often almost powerless, and the arms may become so weak that with the ataxia of the movements that are possible the patient may be quite helpless.

The condition of the muscular tone depends on the relative amount of the degeneration of the posterior roots and of the pyramidal tracts; as a rule the limbs are flaccid and hypotonic, but they are occasionally rather rigid, and even reflex spasms of the legs have been observed

(Everett Smith). Contractures are rare, but have been described by Noica and others. The size of the muscles generally remains fair despite their inactivity till the later stages, but occasionally there is local atrophy, either of the muscles of the legs or of the small muscles of the hand. An interesting group of cases in which Friedreich's disease is combined with a primary muscular dystrophy has been observed by Ghilarducci, Baümlin (68), and Kollarits. Ghilarducci records in five generations of the one family 25 cases, of which he examined four. The myopathic changes were characteristic, but it seems doubtful if the other symptoms justified the additional diagnosis of Friedreich's disease. In Baümlin's case, in which there was pseudo-hypertrophy of the muscles of the shoulders and upper arms, the spinal changes characteristic of Friedreich's disease were afterwards found by Bing; a brother of this case had the typical symptoms of Friedreich's disease. Kollarits' case presented the symptoms of both myopathy and of hereditary ataxia, but the spinal lesions were confined to the dorsal columns and the pyramidal tracts.

The absence of sensory troubles is generally included in the classical features of the disease, but it is not at all rare to find some blunting of cutaneous sensibility on the distal segments of the limbs, especially on the legs, in the advanced stages of the disease at least. Soca found anaesthesia recorded in almost half the 61 cases he analysed. As a rule sensibility to touch, pain, and temperature is about equally diminished (Noica); the borders of the hypaesthetic areas are indefinite, and the loss gradually diminishes towards the hip and shoulder; it does not correspond to cutaneous root-areas as in tabes.

It is of interest that in many of the cases that have been recently examined some loss of the sense of position has been detected in the legs, and occasionally also in the arms. This form of sensation is also more disturbed in the peripheral than in the proximal segments of the limbs. Egger observed constantly loss or diminution of osseous sensibility to a slowly vibrating tuning-fork. The combined loss of cutaneous and deep sensibility may lead to a difficulty in recognising the form of objects by touch, or astercognosis.

Subjective sensory disturbances are also generally absent, but occasionally patients complain of numbness or tingling in the hands or feet. Many authorities, as Ladame, would summarily exclude all cases in which there occur tabetic-like lightning pains, but the association of such pains with the characteristic signs of the disease in one member only of a family in which other members are also affected makes this attitude unreasonable. In a few families, as in that reported by Dr. H. Bramwell, in one member of which the clinical diagnosis was confirmed by necropsy, lightning pains in the limbs were prominent. Cramp-like pains have been also described, and a girdle-sensation was present in one of Dr. Ormerod's cases. Bonnus has found loss of testicular sensation.

The functions of the cranial nerves are rarely prominently affected. Nystagmus is present in many cases, especially in the advanced stages of the disease, but it usually appears only on volitional movement of the

eyes, chiefly with the conjugate lateral movements. It is generally fine and regular, but is often represented only by irregular nystagmoid jerking. It cannot be regarded as one of the essential symptoms of the disease, and the reluctance to make a diagnosis in its absence is quite unjustifiable.

The ocular movements are almost invariably intact, but there is occasionally a history of diplopia, and strabismus and ptosis have been observed. The pupillary reflexes remain active, though cases have been recorded by Philippe and Oberthür, and by Lhermitte and Artom, in which there was loss of the reflex to light; the former case, however, developed after infection with syphilis. Almost all authorities state that the optic discs are invariably normal, but optic atrophy has been observed (Ormerod, Taylor, Cohn, and Breton and Painblan). All these cases were otherwise typical, and those seen by Drs. Ormerod and Taylor occurred in families in which other members had the characteristic signs of Friedreich's disease, but not optic atrophy.

Articulation is almost always impaired except early in the disease; it becomes indistinct and slurred, the syllables are separated, and the utterance is almost characteristically explosive. Even the movements of respiration become irregular and ataxic, and there often occur curious short inspiratory whoops. Abductor palsy of the vocal cords has been observed (Purves Stewart). There is probably no other disease in which the facial movements are so ataxic; this is easily observed in conversation, as not only the lips and cheeks, but even the muscles of the forehead, may be seen undergoing irregular and purposeless contractions.

Progressive deafness has been described in 3 cases by Christiansen, but hearing is rarely affected; vertigo, however, is often a prominent symptom even in the early stages of the disease. The movements of the tongue and the act of swallowing are not affected.

The sphincters usually escape, but in a few of the recorded cases there has been a defective control of the vesical sphincter, or a difficulty in starting micturition.

One of the most characteristic features of the disease is the absence of the tendon-reflexes, but this is by no means an absolute rule. In many families the loss of the knee-jerk is the first objective sign of the disease; thus, they may be absent in the younger members of a generation in whom there is yet no ataxia of gait (Judson Bury). In other cases the knee-jerks have been observed to disappear during the evolution of the disease. Finally, in many cases in which the diagnosis cannot be questioned the knee-jerks have persisted into advanced stages of the disease, or they have been present in some of the members of an affected family though absent in others. In some of these cases the clinical diagnosis has been verified by necropsy. Nolan and Howard Gladstone observed ankle-clonus. The tendon-jerks of the arms disappear as a rule later than those of the lower limbs. The superficial reflexes of the abdomen gradually diminish, whilst the plantar reflex is almost invariably an extensor response (Babinski's sign).



Characteristic skeletal deformities are frequently present; lateral curvature of the spine is common, and it is often associated with some kyphosis. Deformity of the feet is still more common; sometimes it is a simple talipes equino-varus, but the feet are often in addition shortened and clubbed, the plantar arch as seen from the inner side is abnormally high, the balls of the toes are unduly prominent, and the toes are over-extended at the metacarpophalangeal joints but flexed at the interphalangeal joints. The great toes thus assume a Z-shaped position. Any one of these features may be present alone. The fingers are apt to be over-extended at the basal joints, but lie in the position of moderate flexion at the interphalangeal joints, and the hands thus assume the position of a flattened *main en griffe*.



FIG. 91.—The spinal deformity in Friedrich's disease.



FIG. 92.—The characteristic deformity of the feet in Friedrich's disease.

It seems doubtful if visceral crises should be included in the clinical picture of the disease, but Dr. H. Bramwell's case had attacks of gastric pain and vomiting lasting as long as forty-eight hours, which appear to have been true gastric crises; a brother of this patient had attacks of intestinal pain and diarrhoea; and similar cases have been observed (Ormerod (44), Michell Clarke). Periodic attacks of dyspnoea were noted by Fürstner.

Trophic and vasomotor disturbances are rarely prominent, but occasionally there are cold and livid hands and feet, and even oedema and local cyanosis; probably they are largely a result of the inactivity necessitated by the disease. Little is known of the state of sexual power, except that women have borne children in the advanced stages of the disease, and one of Dr. Tresidder's patients begat a son when he was

almost bedridden. Dr. Newton Pitt originally drew attention to the frequent coexistence of cardiac and vascular disease. Congenital disease of the heart, generally pulmonary stenosis (Aubertin), has been found in a large number of cases. Lannois and Porot emphasise the frequency of a degenerative myocarditis, which they attribute to an infection to which a family idiosyncrasy leaves the patient unduly susceptible. Thickening of the walls of the peripheral vessels, generally due to periarteritis, has been frequently found on necropsy. These cardiac lesions are probably responsible for the tachycardia and arrhythmia, as well as the syncopal attacks which are frequently observed in Friedreich's disease; though Guenot and others would attribute them to sclerosis of the grey matter of the floor of the fourth ventricle.

Intelligence is seldom seriously impaired, but many patients gradually become dull and childish, and are remarkably indifferent to the steady progress of their malady. Nolan and Pritzsche have observed the disease in association with progressive idiocy, and Degenkolb a case in a Mongolian idiot.

The *course* of the disease unfortunately is progressive, and there is no evidence that it ever becomes permanently arrested. Little, however, is known of the fate of those younger members of affected families who may be found to present absence of the knee-jerks or other isolated signs. As the gait becomes more seriously affected the patient is bedridden, and may eventually lose almost all power of movement in the limbs. The ataxia of the arms increases more slowly and the weakness rarely becomes so extreme, but many patients survive for years in an absolutely helpless state. It must be remembered that the power of walking is not infrequently lost, or deteriorates seriously while a patient is confined to bed, either in the course of treatment or by some adventitious illness. Febrile and infective diseases frequently accelerate the course of the malady.

The disease itself rarely shortens life, though sudden collapse and death from cardiac failure, due to the coincident myocardial or valvular disease, is not infrequent. And the patients enfeebled by inactivity often fall easy victims to intercurrent maladies.

**Treatment** can effect but little, as the disease is always progressive and its arrest beyond our power. Systematic tonic treatment, however, often produces considerable results; the gait, for instance, often improves remarkably with the improvement of the general condition. Exercises for the re-education of movement, as those devised by Frenkel for the treatment of tabes, may appreciably diminish the ataxia. Massage and electrical treatment should also be tried.

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II. SPINO-CEREBELLAR ATAXIA.—**Definition.**—A chronic slowly progressive disease with gradual and insidious onset, which is generally hereditary, though many sporadic cases must be included in it. It is characterised by a gradually increasing inco-ordination of voluntary movement, which usually affects the legs first, but gradually attacks the arms, the movements of the head and face, and the organs of speech. Other adventitious or accessory symptoms, such as optic atrophy, may supervene. The essential structural lesion is a primary degeneration of the spino-cerebellar tracts.

**Morbid Anatomy.**—There are few necropsies on typical cases as yet available. The spinal cord has usually been found to be unnaturally small, but the most prominent change in it has been a primary degeneration of the spino-cerebellar tracts, especially of the direct cerebellar tract; Gowers' tract has been found less affected. In most of the cases there has also been a certain amount of degeneration of the dorsal



columns of the spinal cord, chiefly in the middle root-zones of the lower segments, but it is insignificant when compared with the degeneration of these tracts in Friedreich's disease. The pyramidal tracts usually escape. In some of the cases the brain-stem and cerebellum were small in proportion to the cerebrum, but no definite degenerative changes have been found in them.

**Symptoms.**—Males and females seem to be equally affected. The hereditary nature of the disease is usually a prominent feature; Sanger Brown observed 25 cases in five generations of a family, Neff 13 cases in four generations, and Lennmalm traced a disease with these symptoms through eight generations. It seems to be more commonly transmitted through females than through males.

The onset is generally later in life than in Friedreich's disease; in the majority of Sanger Brown's cases, and in most of the others, it began between seventeen and thirty-five years of age, but in Neff's cases the symptoms did not appear until about sixty. Its hereditary and familial nature is strong evidence that the disease is due to congenital or intrinsic causes, but infectious illnesses, pregnancy, and other depressing influences may determine the onset or aggravate the symptoms already present. The symptoms come on slowly and insidiously, and increase gradually in intensity and number. The ataxia generally first manifests itself in walking; gait becomes irregular and staggering, and not infrequently it is described as like that of a drunken man. The patient stumbles and reels from side to side, but as a rule avoids falls despite the evident difficulty there is in maintaining equilibrium; the gait has thus all the characters of that form which is usually described as cerebellar. As he becomes more affected with advancing years the patient is unable to walk without support and is finally bedridden. In some cases there is some weakness and rigidity of the legs in the advanced stages of the disease, and spastic contractures have been observed. The movements of the upper limbs become ataxic later than those of the legs, but their finer movements eventually become impossible or extremely inefficient. In many of the recorded cases there has been a notable slowness and sluggishness of all voluntary movement; they are slowly initiated and, as it were, performed with great deliberation.

Static ataxia is also a prominent symptom when the disease is fully developed; there are irregular choreiform movements or constant tremors of the head, trunk, and limbs whenever an attempt is made to maintain these parts unsupported in a fixed attitude by muscular effort. These irregular spontaneous movements cease when the parts are fully supported and during sleep.

The functions of the cranial nerves are equally affected, but they are generally involved at a later date. Ptosis was observed by Sanger Brown, diplopia was present in many other cases, and in some there were extensive ocular palsies. Nystagmus seems to be rare. The pupillary reactions are generally intact, but the contraction to light is sluggish or even lost in the cases in which optic atrophy occurs. Optic atrophy,

with concentric narrowing of the fields of vision, occurs in a large proportion of the familial cases, and may be an early sign; it may lead in time to serious deterioration of vision.

Disturbance of articulation is another prominent symptom; speech becomes indistinct, slurred, and jerky, evidently due to inco-ordination of the muscles of phonation and articulation. A difficulty in swallowing and drinking which has been occasionally observed is probably due to ataxia and not to weakness of the muscles concerned in these actions. The face is often peculiarly immobile, and its expression heavy and stolid, owing to the relaxation of the facial muscles; their inco-ordination is represented by the irregular, excessive, and purposeless contractions that accompany the facial movements incidental to articulation and expression.

Sensory symptoms are usually absent and never prominent. In a few of the cases (Klippel and Durante) there were severe sharp pains in the legs, but the pains due to cramps are more common. Cutaneous sensibility is not disturbed in the typical cases, and the sense of position is invariably intact.

The knee-jerks and the other tendon-reflexes are usually exaggerated except in the late stages of the disease. Ankle-clonus has been described. The sphincters are rarely affected, and then only in the advanced stages.

Skeletal deformities, apart from those due to contracture of the muscles of the lower limbs, do not occur, nor do vasomotor or trophic symptoms. Serious mental deterioration is not characteristic, though in Neff's cases the disease was associated with a terminal dementia.

In addition to incapacitating the patient, the disease seems occasionally to produce progressive emaciation and exhaustion; in some of Sanger Brown's cases death seemed to result directly from these causes.

**Diagnosis.**—It is difficult to give the data on which the diagnosis can be definitely made, for the disease as here described is only a clinical type of which we know little as yet. This is especially so in attempting its distinction from Friedreich's disease, of which it may be regarded as merely a variety, and to which it is connected by intermediate cases. From typical cases of *Friedreich's disease* spino-cerebellar ataxia is distinguished by its onset at a later age, a greater tendency to its hereditary transmission, the persistence or increase of the tendon-jerks, the absence of skeletal deformities, the more irregular character of the gait, and the frequent occurrence of optic atrophy and ophthalmoplegia.

From *disseminated sclerosis*, which many of the cases resemble closely, it may be separated by its more uniformly progressive course, the absence of true spastic symptoms and of sphincter trouble, and by the fact that the affection of vision is not due to retro-bulbar neuritis producing central scotomas, as it is in the majority of the cases of disseminated sclerosis. The diagnosis is especially difficult from the familial cases of disseminated sclerosis, such as have been described by Eichhorst and others.

**Prognosis.**—The disease seems to have invariably a steadily progressive course, but it has little tendency to shorten life. The rate of progress is variable; in some families those affected are crippled within

a few years, but in other cases not till years after the onset of the symptoms.

**Treatment.**—No method of treatment is known to influence the course of the disease. Attempts should be made to reduce the ataxia, the most troublesome symptom, by the re-education of movement, but brilliant results cannot be expected.

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III. CEREBELLAR ATAXIA.—Though cerebellar symptoms frequently result from focal lesions, primary degenerative disease of the cerebellum is very rare. It occurs occasionally, however, as an hereditary or familial disease.

In these cases it is generally the cortex that is involved; and, as it is in the cortex that the chief afferent tracts to the cerebellum terminate, this form of disease is closely related to those in which the afferent tracts to the cerebellum are affected, that is spino-cerebellar ataxia and Friedreich's disease. In fact Menzel, Perrero, Bing, and Thomas (101) have described cerebellar atrophy associated with the spinal lesions of Friedreich's disease. Raymond and Lhermitte, as well as Stelzner, have also recorded families in which the disease could be traced through three generations; the cases in which a necropsy was possible shewed, in addition to a general atrophy of the cerebellum, a degeneration of the dorsal columns of the spinal cord and of the spino-cerebellar tracts, but the pyramidal tracts were intact.

The cause of this cerebellar degeneration must be sought in a congenital or hereditary anomaly in the constitution of the systems of neurons which degenerate in later life. Extrinsic factors seem to have little influence in determining the onset or course of the disease, though Murri and Rossi have observed cerebellar degeneration secondary to intestinal infections.

**Morbid Anatomy.**—In a family in which I observed the disease four members were affected. The sole pathological lesion was a degeneration of the cortex of the cerebellum, and of the fibres which connect this with



the central nuclei; the efferent cerebellar tracts were intact, as well as all the afferent tracts except the olivo-cerebellar fibres. The whole cerebellum was scarcely more than a third of the normal size. In the one of Dr. Fraser's cases that was examined (in this family a brother and a sister were affected), the pathological changes were similar, but in Thomas's case there was only atrophy and disappearance of the Purkinje cells of the cortex.

These cases must not be confused with those in which there is merely agenesis or developmental defect of the whole or part of the cerebellum; in these there may not be any symptoms, or there may be ataxia, tremor, and other signs of cerebellar disease from birth (Vol. VIII. p. 136). This form of cerebellar agenesis is often associated with imbecility or epilepsy. Progressive cerebellar disease due to vascular or interstitial lesions must be also distinguished from this form of familial cerebellar degeneration.

**Symptoms.**—In the family with four members affected under my observation, the disease set in between thirty and forty years of age; in other cases it has appeared in earlier life. The first and most prominent symptom is that gait becomes irregular and the patient begins to stagger and reel from side to side, deviating widely from the line of progression like a drunken man. Equilibration is seriously affected, and falls frequently result in the attempt to avoid or surmount obstacles. Romberg's sign is not present; the unsteadiness does not become greater when the patient closes his eyes. The movements of the arms become ataxic simultaneously or later; there are wide and purposeless deviations from the direct line of movement, and finer actions, such as sewing and writing, soon become impossible. Tremor and irregular choreiform movements of the limbs and head are constantly present when these parts are not fully supported. Articulation gradually becomes hesitating, scanning, and explosive. The pupillary reflexes persist and ocular palsies do not appear, though nystagmus, or irregular nystagmoid jerking of the eyes on movement, are very common. There was optic atrophy in one of Dr. Fraser's cases. Sensibility is unaffected, and the reflexes and sphincter functions remain intact. The disease is slowly progressive, and no form of treatment can influence its course.

**Olivo-Ponto-Cerebellar Atrophy.**—A special form of primary cerebellar disease which is characterised by atrophy of the cerebellar cortex, the bulbar olives and the grey matter of the pons, with degeneration of the middle peduncles of the cerebellum, has received the name *olivo-ponto-cerebellar atrophy* from Dejerine and Thomas. It is not, however, an hereditary or familial disease.

It sets in late in life, generally in the sixth decade, and progresses slowly. The most prominent symptoms are difficulty in maintaining equilibrium in standing and walking, and a reeling and staggering gait of the cerebellar type. The individual movements of the lower limbs are, however, usually fairly well co-ordinated. There is also ataxia of the arms, and irregularity of their movements of the intention-tremor type; tremor or choreiform movements of the limbs may be also observed.

Articulation becomes slow and scanning, and nystagmus is usually present. Slight paresis and spasticity of the legs have been observed, and in some cases the tendon-reflexes have been exaggerated.

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### SUBACUTE COMBINED DEGENERATION

SYNONYMS.—*Anämische Spinalerkrankung* (Nonne); *Subacute Diffuse Degeneration of the Spinal Cord* (Burr and MacCarthy).

By JAMES COLLIER, M.D., F.R.C.P.

**Short Description.**—A disease of insidious onset, usually occurring in the fifth or sixth decade of life, which invariably progresses without pause to a fatal result in from three months to four years. The clinical manifestations are strikingly distinct, the early stages of the disease being marked by peripheral paraesthesias, the later stages by spastic or flaccid paraplegia and ataxia, and the latest stages by loss of sensibility of unusual and peculiar distribution, in that it is a paranaesthesia and a "stocking and glove" anaesthesia combined. In the late stages of the disease the paraplegia tends to be complete, and is often flaccid with loss of the deep reflexes. Severe secondary anaemia is almost invariably present at some period of the disease, sometimes preceding the appearance of nervous symptoms by many months, sometimes coming on coincidentally with them, and more rarely being deferred till the last stages of the disease.

**History.**—The earliest recorded cases were those published in 1884 by Leichtenstern as "progressive pernicious anaemia in tabetic patients"; in the same year Lichtheim reported pathological changes in the spinal

cord in cases of severe anaemia. In 1886 Sir W. Gowers described a new clinical entity which he called "ataxic paraplegia"; but in the light of subsequent investigation it now seems clear that the cases upon which he based the morbid anatomy of this condition were examples of subacute combined degeneration, and that many of his clinical cases belonged to the spinal form of disseminated sclerosis, which at that time was little recognised.

Following the results of Lichtheim's researches, Bowman, Burr, Minnich, Nonne, and James Taylor, who recorded cases, regarded the anaemia as an essential feature of the disease and as the cause of the lesions of the spinal cord and of the nervous symptoms. Considerable confusion thus arose, since on the one hand the cases without conspicuous anaemia were not recognised, and on the other hand a fundamentally distinct clinical group was included which has no connexion with subacute combined degeneration. This group comprises cases of severe anaemia in which pathological changes are found after death in the spinal cord. Many of these cases do not present symptoms of nervous lesions, whilst the others shew irregular signs of slight implication of the spinal cord late in the course of grave anaemia. It is highly probable that these changes in the spinal cord are directly due to the anaemia, whereas in subacute combined degeneration the anaemia and the spinal lesions are certainly not in the relation of cause and effect, but are concomitant or sequential results of the same cause. Following the publication of 3 cases with pathological verification by Dr. Risien Russell in 1898, the peculiar clinical features of the malady were for the first time pointed out with certainty and placed upon a firm basis by Risien Russell, Batten, and Collier, who recorded 7 cases in which the diagnosis had been definitely made in the early stage of the disease and confirmed by necropsy. Subsequent investigation has shewn that the three definite clinical stages of the disease, described by these writers, are not present in many of the cases; and an increasing knowledge of the variability of the clinical aspect has necessitated the abandonment of definite clinical stages in the description of the disease and the broadening of the clinical picture. In 1901 Brown, Langdon, and Wolfstein in America published a monograph entitled "Combined Sclerosis of Lichtheim-Putnam-Dana Type, accompanying Pernicious Anaemia"; and in 1903 Burr and MacCarthy classified the postero-lateral sclerosis of the spinal cord, and described this disease as "subacute diffuse degeneration." Numerous cases have been recorded since, especially by C. S. Potts in 1905 and by J. Grinker, who published a clinical and pathological description of 17 cases in 1908. Crouzon of Paris in 1904 devoted his thesis to this subject, and subsequently published a pathological investigation. All recent writers have accepted the title "subacute combined degeneration," originally suggested by Risien Russell, Batten, and Collier in 1900.

**Etiology.—Age.**—The extremes at which the onset of the disease has been recorded are thirty and sixty-five years of age. A few cases have occurred between thirty and forty, but during the succeeding decade



they become increasingly numerous, and the highest incidence is reached between the ages of fifty-five and sixty years. In the younger subjects the disease is apt to be more acute and its course more rapid.

In the *sexes* the incidence appears to be equal at all ages. *Hereditary influences* do not appear to play any part, though a family disposition to nervous disease, tuberculous affections, rheumatic fever, or cancer has been present in several cases.

Little is known of the causal factors of the disease, and in a majority of recorded cases the patients have been strong and healthy until shortly before the onset of symptoms. A definite history of syphilis has been found in a good many of the cases. In a few instances alcoholic excess, and in others prolonged suppuration or nephritis, has immediately preceded the onset. In three recorded cases the disease followed immediately upon a normal puerperal state. Two patients under my care lived in adjoining houses in the same street. Otherwise no connexion can be traced between the disease and acute illness or emotional disturbance.

Dr. William Hunter has insisted on the importance of oral and intestinal sepsis in the causation of profound anaemia. These conditions are common in subacute combined degeneration when the disease is well advanced, and increased intestinal disturbance has not infrequently been noticed to correspond with exacerbations both of the anaemia and of the nervous symptoms; but a history of intestinal sepsis or illness before the onset of the disease has hitherto been sought for in vain.

**Morbid Anatomy.**—The essential lesion is confined to the white matter of the spinal cord and brain-stem, and in the early stages to definite regions of the white matter. The grey matter is unaffected except for the changes in the nerve-cells resulting from the destruction of certain tracts in the white matter. The cytology of the cerebrospinal fluid does not present any special feature. The meninges and the anterior and posterior roots are normal. The superficial macroscopic appearance of the spinal cord departs but little from the normal, and diminution in its size is seen only in very prolonged cases; in this respect the disease differs widely from other forms of postero-lateral and scattered sclerosis, in which shrinking of the cord is always conspicuous. In transverse section of the cord the degenerated areas are seen as spots of a darker and more translucent appearance than the normal white matter. They usually appear first in the mid-dorsal region, where they are most extensive throughout the disease. The degeneration always commences in definite regions of the cord as seen on transverse section, and small areas appear first in the centre of either posterior column, soon after in the centre of both lateral columns in the position of the pyramidal tract, and at this stage of the disease only is the anatomical picture one of strict postero-lateral degeneration, for a little later spots of degeneration appear on either side of the anterior median fissure, and later still in any position in the white matter in the anterior columns. The degenerate areas gradually increase in size centrifugally, and reaching the surface of the cord, at the later stages of the disease, eventually involve the whole of the white

matter of the cord as seen on transverse section except the narrow zone of short internuncial fibres which everywhere clothe the grey matter. The anatomical picture at this stage is highly distinctive; the intact grey matter covered with a thin layer of normal white fibres and the complete



FIG. 93.—Photomicrographs of transverse sections of the spinal cord in subacute combined degeneration, stained by Weigert's method. The lower figure, from the mid-dorsal region, shews the characteristic degeneration of the lateral and posterior columns. Recent small spots of degeneration are seen in the anterior and posterior columns; and in the anterior part of the left lateral column a small spot of degeneration is seen fusing with the main area of degeneration. The upper figure, from the mid-cervical region, shews clearly the ascending secondary degenerations in Goll's column and in the direct cerebellar tract, in addition to the commencing focal degeneration in the posterior, lateral, and anterior columns.

degeneration of the rest of the white matter without conspicuous shrinking of the cord give the picture of an "annular" or "ferrule-like" lesion which does not occur in any other disease.

From its starting-point in the lower dorsal region the disease spreads upwards and downwards in the spinal cord, and longitudinal sections of the spinal cord shew clearly that this extension depends on the

occurrence of small, isolated spots of degeneration, in the posterior, lateral, and anterior columns, which increase in size and thus join the areas previously degenerated. Though in its earlier stages the disease is confined to definite regions of the white matter, it does not resemble a system disease of the spinal cord, as it advances by the formation and coalescence of separate small focal lesions. The appearance of the lesions will vary according to the duration of the illness; for example, in a case which has proved fatal in a short time the lesions in the lower dorsal region will probably be confined to the posterior columns, the region of the crossed pyramidal tracts and the region of the direct pyramidal tracts, and the lesions may not reach the surface of the cord, whilst as the degeneration is traced towards the cervical region it becomes smaller in area and more confined to the centre of the posterior and lateral columns respectively. Traced still further, the degeneration will be found no longer continuous but in the form of small isolated spots. On the other hand in a case which has run a long course after the paralysis has become severe, the whole of the dorsal region will shew complete "annular" degeneration of the white matter, the short fibres which clothe the grey matter alone escaping; whilst the cervical region shews a condition similar to that seen in the earlier stages in the dorsal region, the posterior and lateral columns alone being affected. The degeneration usually does not extend higher than the lower part of the medulla; in a few cases, however, it has been met with as high as the centre of the pons, and in these two situations the spots of degeneration are always in the pyramidal tract.

The essential lesions of subacute combined degeneration, small foci of degeneration which extend and run together and invariably appear first in the centre of the posterior and lateral columns, induce two series of secondary lesions which depend upon the destruction of the axis-cylinders in the degenerate areas. The first group comprises the secondary degenerations of the ascending and descending tracts of the spinal cord, such as occur from every local lesion of the cord in which the axis-cylinders are destroyed. The primary lesions in the posterior and lateral columns early entail secondary degeneration in Goll's column, in the lateral pyramidal tract, and in the posterior descending system; subsequently, when the rest of the white matter in the lower dorsal region is involved, the two spino-cerebellar tracts, the spino-tectal, and the spino-thalamic systems undergo secondary degeneration throughout their course. The other group of secondary changes are the retrograde lesions of tigrolysis, vacuolation, and shrinking which occur in certain groups of the nerve-cells from the destruction of their axons by the lesions of the white matter of the spinal cord. These changes are conspicuous in the cells of Clarke's column, as the result of the interruption of the spino-cerebellar tracts, and in the pyramidal cells (cells of Betz) of the ascending frontal gyrus, in consequence of the interference with the pyramidal tract in the spinal cord.

During the evolution of the essential focal destructive lesions the



following sequence of changes can be seen:—The earliest is swelling of the medullary sheaths over a small area of the white matter. The swollen sheaths then break by fatty degeneration and the axis-cylinders become no longer recognisable. The degenerate contents of the swollen medullary sheaths now disappear, leaving nothing but the fine connective-tissue of the spinal cord surrounding vacuolated spaces of varying size, many of which are formed by the fusion of several such spaces, whilst some represent the spaces originally occupied by the nerve-fibres. Later on there is neuroglial increase in the vacuolated area, which in prolonged cases may reach a considerable density. From the edge of a focal lesion once formed the same series of changes spreads centrifugally, until the lesion fuses with another, or reaches the surface of the cord on the one hand or the short white fibres clothing the grey matter on the other hand.

The blood-vessels of the white matter sometimes shew fatty changes and occasionally sclerosis, but as these changes are only marked in regions where the destructive process is advanced they are presumably the result of the destructive process. In two cases I found multiple small haemorrhages, which were all recent, scattered throughout the white matter.

The brain does not shew any abnormality other than the cell-changes above described, but where the patient has survived for long, and general nutrition has been severely affected, there may be considerable shrinking of its bulk with corresponding increase of the subarachnoid fluid.

The peripheral nerves are unaffected. The muscles throughout the body are wasted, especially in the regions where paralysis has been complete for long, and in such cases the muscle-fibres are reduced in size, even to 4  $\mu$ , and have lost their striation. The atrophied muscle-fibres are in striking contrast to the nerve-fibres within the muscle, and this condition is strictly comparable to that seen in prolonged cases of total transverse lesion of the spinal cord.

*Blood.*—In a few instances anaemia has been absent throughout, the haemoglobin and the cytology being normal; this occurs in cases which have run an acute and fatal course in a few months. Usually the blood shews a secondary anaemia of varying severity; the haemoglobin ranges from 35 to 75 per cent, the lower of these figures being common; the colour-index is usually above the normal, and may be as high as 1.6. Anisocytosis, poikilocytosis, and polychromatophilia are common. Normoblasts are sometimes numerous, but megaloblasts have not been found. The leucocyte-count is normal, unless some suppurative complication supervenes. The reaction for free iron in the liver has not been obtained in any case (*vide* Vol. V. p. 731). In the alimentary canal septic gingivitis and stomatitis are common, signs of chronic gastro-enteritis and colitis are occasionally present, and more rarely there are small ulcers in the large intestine.

*Pathology.*—The early writers believed that the anaemia was an essential part of the disease, and that the changes in the spinal cord were the results of vascular changes consequent upon the anaemia. The discovery

that vascular lesions of the spinal cord, such as small haemorrhages and small points of softening, are sometimes found in the terminal stages of any severe anaemia gave some support to this belief. These lesions, however, have occurred only as terminal phenomena in the course of severe anaemia, and the clinical manifestations of the spinal lesions have been generally slight and often absent. In 2 cases I found multiple small haemorrhages in the spinal cord. They were all recent, were irregularly distributed throughout both grey and white matter, and could not be correlated with any clinical phenomena. They had evidently occurred shortly before death, and their distribution had no relation to the characteristic lesions of subacute degeneration present in these cases. The unvarying commencement and extension of the pathological change in definite regions of the white matter only of the spinal cord, its extension by the coalescence of contiguous small foci, and the absence of any histological evidence of haemorrhage, thrombosis, or of changes in the vessel-walls in the early stages of the lesions, are quite incompatible with a vascular origin. Moreover, the anaemic states especially associated with the occurrence of haemorrhage do not present either the clinical or the pathological features of subacute combined degeneration; and conversely the anaemia of this disease is not conspicuously associated with the occurrence of haemorrhages. Further, clinical data militate against the view that the changes in the spinal cord are due to the anaemia, for some cases never present any anaemia and yet usually run a rapid course. In other cases the anaemia does not appear till the nervous manifestations are well advanced, and in no case can it be said that there is any strict relation between the degree of the anaemia and the severity of the spinal lesions. Obviously, however, the failure of tissue nutrition accompanying the anaemia may facilitate the occurrence of the spinal degeneration.

The anaemia and the spinal degeneration are therefore related, not as cause and effect, but as concomitant effects of a single fundamental pathological process which in the present state of knowledge must be hypothetical. Notwithstanding these considerations, Nonne, who was an early exponent of the anaemic hypothesis, has maintained his original contention, and in 1908 described the essential lesion as a focal myelitis, caused by changes in the vessel-walls of certain definite regions of the spinal cord, and stated that the vascular changes depend on the anaemia, and may arise in any form of anaemia. It may be pointed out that the entire absence of inflammatory cells in the early lesions militates against the notion that the condition is a myelitis, and also that the changes in the vascular walls are inconspicuous in the early stages of the lesion, and become more marked as the degeneration of an area becomes profound. Such alteration of the vessel-walls is an inevitable consequence of parenchymatous degeneration of the white matter. That the distribution of the spinal degeneration is to some extent determined by the vascular supply is certain. The area supplied by the anterior spinal artery is never involved, namely the grey matter and the layer of white

fibres (largely endogenous) which everywhere ensheath it. It is quite clear that the distribution of the degeneration in the area of supply of the posterior spinal arteries and radicular arteries is not determined by any condition of meningitis that might interfere with these vessels as they enter the surface of the cord. Further, the areas of degeneration appear to have no relation to vascular distribution, their point of commencement being usually the central regions of the posterior and lateral columns, regions which are farthest from the grey matter on the one hand and the surface of the cord on the other hand. It is interesting to note that the disease most often commences in, and throughout its course is most intense in, the mid-dorsal region, which is the part of the spinal cord considered to have the poorest blood-supply and in which thrombotic lesions are most common.

The symptoms and the variations in the clinical aspect of the disease fall exactly into line with the morbid changes. The common ataxic and spastic type corresponds with the commencement and major incidence of the degeneration in the posterior and lateral columns of the mid-dorsal region, the prominence of the ataxia or spasticity in the symptom-group depending upon the extent of the lesion in these two positions respectively. The cases in which flaccidity and loss of the deep reflexes in the lower extremities exist from the first or appear early correspond with an early and major incidence of the degeneration in the posterior columns of the lumbar region, as has been proved in several instances. In the rare cases in which the symptoms have appeared first in the upper extremities, the greater pathological involvement of the cervical region throughout has been demonstrated. The clinical change from the spastic to the flaccid paraplegia which occurs in the late stages of many of the cases is probably coincident with the destruction of all the axis-cylinders of the long descending white tracts in the cord; whilst the continuance of the spastic state to the end depends upon the preservation of some of these axis-cylinders.

The functional character of the paraplegia in the earliest stages of the disease may be due to the presence of incipient lesions before the actual destruction of axis-cylinders, and be thus strictly comparable with the similar functional manifestations which occur in the early stages of disseminated sclerosis.

Both the clinical and the pathological features suggest the existence of some toxic agent which is responsible on the one hand for the anaemia and the cachexia, and on the other for the spinal degenerations. It is possible that more than one toxic agent may work this result, as is suggested by the few known pathological conditions which have existed prior to the onset of the disease. From the experimental work and the hypotheses that have arisen in connexion with the profound anaemias it is natural to consider the possibility that some condition of chronic intestinal infection is responsible for the toxic agent. The clinical evidence, though slight, is in support of this hypothesis rather than against it. No toxic agent, however, has been isolated, no micro-



organism of a specific nature has been found, and treatment based upon this hypothesis has availed nothing in modifying or arresting the course of the disease.

**Onset.**—In a large majority of instances the symptoms appear insidiously and without any attributable exciting cause. When anaemia appears before the nervous manifestations, the breathlessness, headache, languor, and palpitation due to anaemia may dominate the clinical picture for months or even for years, and the early nervous symptoms when they appear may be little complained of and easily overlooked. In a few cases the onset has been rapid; and it was associated with pyrexia, vomiting, and malaise in one case, with severe attacks of giddiness in a second case, and with a chill and malaise in two cases. In one case the onset was so rapid as to suggest acute myelitis, and in this case two attacks of temporary paraplegia had preceded the onset by eight months and by four months respectively.

**Symptoms.**—The following account is based upon the analysis of forty-four cases treated during the years 1898-1909 at the National Hospital, and of the majority of the recorded cases.

Though the symptoms of this disease are remarkably distinct, the grouping of the symptoms often varies. The presence of a conspicuous symptom in one case and its absence in another may give rise to what is at first sight a very different clinical picture in the two cases. Moreover, the clinical aspect may completely change in the course of the disease. A knowledge of these variations is all-important in the diagnosis of the disease. They occur in connexion with two features of the disease. The first of these is the anaemia, which may be absent throughout, be the earliest sign, or rapidly appear at any period, the clinical aspect being remarkably changed by the advent of a conspicuous lemon-yellow colour of the skin. It follows therefore that although the presence of conspicuous anaemia is of the greatest aid in diagnosis, its absence is not of negative value. The second variable feature is the paraplegia which may be one of two opposite forms; the common form is an ataxic spastic paraplegia, the less frequent is the tabetic, with ataxic and hypotonic lower extremities, and with loss of the deep reflexes. The tabetic form of paraplegia never changes in the course of the disease, but the spastic form rarely remains unchanged throughout the course of the disease, and at some stage in the disease, generally a late stage though sometimes an early stage, the spastic paraplegia disappears, often rapidly, and gives place to flaccid paraplegia with loss of the deep reflexes. The change from the spastic to the flaccid type sometimes coincides with the appearance of severe anaemia.

The cardinal symptoms are here summarised:—

*Peripheral subjective sensations*, remarkably obtrusive and often of strictly “stocking and glove” distribution upon the limbs.

*Sensory loss*, which commences upon the limbs with peripheral “stocking and glove” distribution, and reaching on to the trunk ascends in segmental distribution.

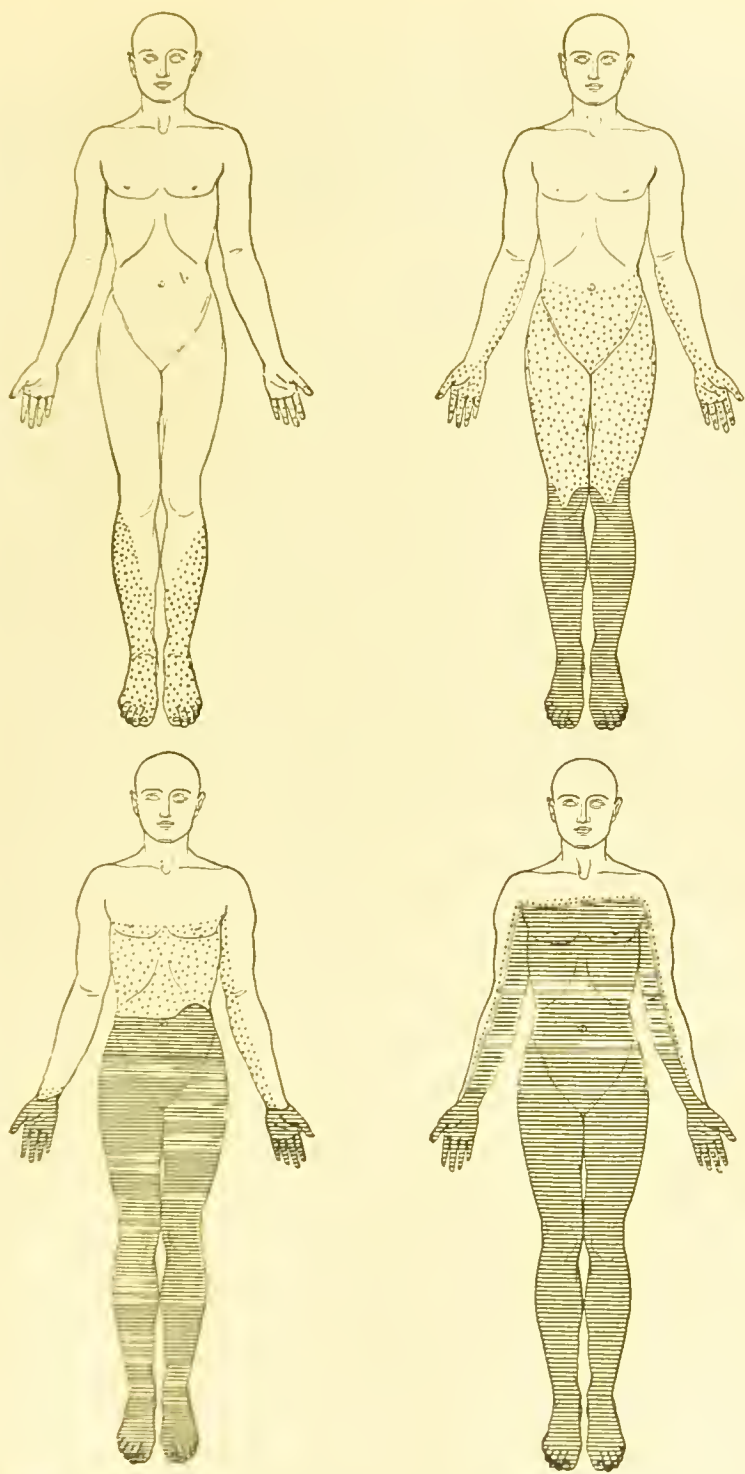


FIG. 94.—Charts of the sensory loss from a case of subacute combined degeneration, shewing the progressive loss as the disease advances. The dotted areas represent partial loss to pain and to temperature; the lined areas represent complete loss to pain and to touch. The first chart shews the sensory loss three months after the commencement of symptoms; the last chart was taken a few days before the fatal event nine months later. The third chart shews a slight temporary improvement in the sensory loss of the right arm.

*Paraplegia*, which may be (a) flaccid from the first with loss of deep reflexes; (b) spastic, remaining spastic throughout (rare); changing to flaccid paralysis, with loss of deep reflexes in late stages (sometimes in early stages). Both forms of paraplegia are accompanied by marked ataxia.

*Girdle sensation. Lightning pains.*

*Muscular wasting* and lowering of electrical excitability, of general distribution in the paraplegic region.

*Sphincter Paralysis*.—Usually of late onset.

*Anaemia*, which may be absent throughout or may become apparent at any period in the course of the disease. It is conspicuous at the time of onset of the nervous symptoms in about one-half of all cases.

*Peripheral subjective sensations*, with a "stocking and glove" distribution upon the limbs, are so constantly the earliest symptoms and are so persistent when they have appeared as to form a most distinctive feature of the malady. These sensations are variously described by the patients, but tingling and numbness without pain form the basis of the paraesthesia in nearly all cases. Sensations of heat, of stiffness of the skin, and of tightness, as if the limb were bandaged, often accompany the numbness. In some instances the first complaint has been of dull aching pain in the limbs, and frequently lightning pains indistinguishable from those of tabes have appeared early and have persisted. These subjective sensations are distributed at first upon the periphery of the limbs, usually in a "stocking or glove" fashion, more rarely in a nerve-root distribution. Most often they are first noticed in the legs, but sometimes they are first felt in the hands. At first peripheral, they subsequently spread towards the trunk, and are followed at a variable interval by loss of sensibility, which commences peripherally, and which has the same distribution ultimately as had the paraesthesia. Extending on to the trunk from the limbs the loss of sensibility is always limited by an intersegmental line, though this is rarely sharp and definite, and upon the limbs it sometimes has a nerve-root distribution. The nature of the sensory loss varies in different patients; generally sensibility to pain is lost earlier and to a greater degree than tactile sensibility, and as the sensory loss spreads from the limbs to the trunk and upwards upon the trunk, the loss to pain precedes the loss to touch. In other cases, however, the tactile loss may precede and exceed the loss to pain, and in rare instances tactile and thermal perception have persisted where perception of pain has disappeared. The muscular sense and sense of position are among the earliest of the sensory perceptions to disappear. In the later stages of the disease the sensory loss is apt to become absolute to all forms of stimuli in proportion to the duration of the illness. For example, in acute cases which rapidly end fatally the sensory loss may be neither extensive nor deep, whereas in chronic cases which have been bed-ridden for months all forms of perception may be abolished up to a high level upon the trunk. The most extensive sensory loss I have seen was one of complete loss to all forms from the fifth cervical segment



downwards, and partial loss over the fifth cervical segment. Such a distribution is not uncommon. A girdle-sensation is the rule and it is sometimes painful, but the time of its appearance is strangely variable; it may be one of the earliest signs, but often it does not appear until the middle or late stages of the disease. Of a similar nature is probably a heavy fixed pain in the hepatic region which has been present in several cases.

At a variable time after the onset of subjective sensory signs spasticity and ataxia of the lower extremities come on, most often insidiously but sometimes rapidly. The patient first finds that his legs are easily tired, that they are stiff, that he drags the feet in walking, that he walks unsteadily in the dark, or that he falls forward into the basin when washing himself. Slight rigidity of the lower extremities with weakness, especially of the dorsi-flexors of the ankle and toes, will be found present with increase of the knee-jerks and ankle-jerks, foot-clonus, a tendency to pes cavus and an extensor type of plantar reflex. The defects of co-ordination are shewn by the loss of sense of passive movement and of position, by ataxia of movement, and by Romberg's sign.

A few cases, however, form an exception to the rule that spastic ataxia is a characteristic feature of the earlier stages of the disease. In these cases the knee-jerk is diminished or lost early, and the clinical picture is one of ataxia with flaccid weakness throughout. Implication of the pyramidal tract is shewn in these flaccid cases by the constant presence of the extensor type of the plantar reflex.

The spastic paraplegia increases in severity as time goes on, but its progress is rarely uniform. Usually a patient shews little increase of the paraplegia for many weeks, and then in the course of a few hours or days a striking and permanent exacerbation of his symptoms occurs. These sudden exacerbations of the symptoms are not unfrequently associated with malaise, pyrexia, vomiting, and other signs of gastro-intestinal disorder, and we may conjecture that there has been a sudden increase in the toxic condition which is responsible for both the anaemia and the spinal degeneration. Temporary remissions of the severity of the paraplegia are very rare, and are associated with striking improvement of the anaemia and of the general health. As the illness advances, the paraplegia involves more and more of the trunk, progressing upwards. The patients lose the power of standing and later of moving the legs, until finally the paraplegia becomes complete, with great wasting of the muscles and great reduction in their faradic excitability. Before the paraplegia becomes complete, the condition of spastic paraplegia usually changes to one of flaccid paraplegia, the rigidity and the foot-clonus departing, and the knee-jerks diminishing and finally disappearing, with persistence of the extensor plantar response. This change often corresponds with the onset of the complete paralysis and of rapid wasting of the muscles in the paraplegic region. But in rare cases the change from the spastic to the flaccid paraplegia occurs quite early in the disease when the paralysis is but slight, and, as we have already seen, some cases

are flaccid from the first. On the other hand, the spastic state sometimes persists to the end in spite of absolute paraplegia and paranaesthesia of months' duration. In such cases of persistent spasticity reflex flexor spasms are a constant and most troublesome feature, and render it impossible for the patient to get any rest. The onset of the flaccid state, like the other exacerbations of symptoms, may be associated with malaise, pyrexia, and gastro-intestinal disturbance, and it is often followed by increase of the anaemia.

The paraplegia does not as a rule reach the upper limits of the regions supplied by the cervical enlargement of the spinal cord. Even in prolonged cases, with complete paralysis of the lower extremities and trunk of many months' duration, the condition of the upper extremities is one of partial paralysis most marked in the periphery, and associated with considerable wasting of the muscles of the hands and forearms.

The electrical excitability of the wasted muscles in the later stages resembles that of the muscles of the paraplegic region in total transverse lesion of the cord. The faradic excitability is much reduced, and is diminished in proportion to the wasting. The galvanic excitability is diminished less than the faradic, and there is not any conspicuous polar change.

The *sphincters* are always affected in the later stages of the disease. Dysuria, rare as an early symptom, generally appears when the paraplegia becomes pronounced, and its appearance is often delayed until remarkably late. When once established it does not shew any tendency to improve with treatment, and incontinence of both the bladder and rectum soon becomes complete, the sphincters remaining patulous. When paraplegia is complete, cystitis cannot be prevented, and if life is prolonged the utmost care and regularity in the lavage of the bladder will not always prevent secondary pyelitis.

*Reflex Action.*—*Superficial Reflexes.*—The abdominal reflexes are usually active, but towards the end of the illness, when the abdomen is retracted, they may be absent. The plantar reflexes assume the extensor type early, and in all probability the extensor response is the first unequivocal sign of organic nervous disease to appear; it always persists to the end. The persistence of a high degree of superficial reflex excitability even in the last stages of the disease is remarkable. The deep reflexes are in most cases increased until the late stages, when with the change from the spastic to the flaccid paraplegia they disappear and remain absent. Exceptionally, they may disappear with the onset of the first symptoms, as in a case under my care in which loss of one knee-jerk preceded other nervous symptoms by several months. The knee- and ankle-jerks, at first increased, may disappear early and while the paraplegia is still slight. The rarest event is for the deep reflexes in the lower extremities to remain excessive to the end; among 44 cases this was noticed three times.

Soft translucent *oedema* of the lower extremities and trunk is frequent, its occurrence often coinciding with an exacerbation of the paraplegia.

It is more marked the greater the anaemia, and obviously depends on the anaemia and on the impaired innervation of the paraplegic region. Severe and painful oedema confined to one upper extremity and disappearing within a few hours has been met with in 3 cases. It is possible that toxæmia may be a factor in the production of oedema.

*The cranial nerves* are rarely affected. Motor paralysis of the face, muscles of mastication, and of the tongue and pharynx has never been reported. In one case, however, troublesome paraesthesia of the tongue was an early and conspicuous symptom (Ginkler). It is conceivable that the degeneration in the cervical region of the cord might reach the ascending trigeminal root and so cause sensory loss over the face, but no instance has as yet been recorded. Diplopia has been reported in one or two cases, and I have twice seen weakness of one external rectus. In these cases no lesion was found to account for the weakness of the sixth nerve. Slight nystagmoid jerkings are often present, and are to be attributed to general debility and inattention rather than to any implication of the cerebellar mechanism.

The pupils are usually small and often unequal; the light-reflex is usually sluggish; complete reflex iridoplegia is not infrequent and may occur even when antecedent syphilis can be practically excluded. The small size and the inequality of the pupils is easily explicable from the degeneration in the cervical region; but the reflex iridoplegia cannot be so explained if the generally accepted view be correct that paralysis of the cervical sympathetic does not entail reflex iridoplegia.

*Special Senses.*—Dimness of vision is common when anaemia and debility are severe. Optic atrophy has been reported in a good many cases, but it is possible that the pallor of the disc, which is striking in some of the anaemic cases, has been confused with optic atrophy, for I have never seen undoubted atrophy of the disc. Slight optic neuritis has occurred in a few cases. It is transient and is doubtless related to the anaemia. Small retinal haemorrhages are occasionally found. No affections of smell and taste have been reported. The mental state in the later stages of the disease is often one of lethargy, drowsiness, and complacency, and is attributable to the anaemia, to the toxic state, and to the profound alteration of general nutrition. In this condition of general bodily depravity delirium is common and general convulsions may occur.

*Anaemia.*—As already pointed out, anaemia may be absent throughout the course of the disease, it may precede the onset of the nervous symptoms, or it may appear at any subsequent time. In more than half the cases it is present at the commencement of the nervous manifestations. The colour of the skin is often striking and approaches lemon-yellow, whilst in the later stages it becomes muddy or clay-coloured. A bright malar flush upon a yellow background sometimes gives a characteristic and vivid facial aspect in the earlier stages. There is no close relation between the reduction of the haemoglobin and the severity of the nervous symptoms. The characters of the blood are described on p. 791.

Temporary improvement may occur in the anaemia as the result of



treatment, but as a rule it gradually increases in severity as time goes on. Some cases, however, that have been anaemic throughout, do not shew a reduction of the haemoglobin below 60 per cent even at the last. Considering the severity of the anaemia in many cases, it is remarkable that haemorrhages should be so rare. Insignificant haemorrhages have been found in a few instances only in the retina, in the posterior-root ganglia producing herpes, and in the skin. The spleen is not enlarged. The symptoms and signs common to all anaemic states, breathlessness, palpitation, headache, cardiac and venous murmurs, and oedema, are usually present; occasionally syncopal attacks occur, but have not proved fatal.

Irregular *pyrexia* is almost invariably present quite apart from complications such as cystitis and bed-sores. It varies from a very occasional elevation of two or three degrees of a temperature, at other times normal, to a highly irregular pyrexia.

*Nutrition.*—Many patients are poorly nourished and cachectic at the onset, but others are fat, and during the earlier stages of the disease may not lose weight but even become fat as in pernicious anaemia. In the late stages, however, progressive emaciation is constant, and if life be prolonged becomes extreme.

Cystitis and bed-sores cannot be avoided in patients who survive long after the onset of complete paralysis, and of paralysis of the sphincters, for the vitality of the tissues seems too low either to resist the advent of micro-organisms, or to allow of any healing process. Death occurs from exhaustion, and but rarely from complications.

The **duration** of the disease varies within wide limits, from six weeks to six years. In the cases of very long duration the symptoms remain slight during a large proportion of the time. Not unfrequently a patient, who has reached the stage at which the disease is usually fatal, survives in a pitiable condition for many weeks or even months. The disease runs its most rapid course in young subjects. Considering all cases together the average duration of the illness from the earliest symptom to the fatal event has been rather more than one year.

**Irregular Cases.**—Under this heading reference must be made to (1) cases which for a short time after the appearance of the symptoms present the aspect of functional paraplegia, (2) cases in which the upper extremities are most affected in the early days of the illness, (3) two cases in which the onset was a sudden paraplegia which passed off in a few weeks and recurred a few weeks later (the subsequent course and the post-mortem changes being characteristic), and (4) the case in which paraesthesia of the tongue was an early and prominent symptom.

**Diagnosis.**—In the earliest stages this is often difficult. Before the appearance of definite signs of organic spinal disease many cases have been regarded as functional paraplegia or neurasthenia. The preponderance of the peripheral subjective sensations and of a florid complexion with anaemia will help to suggest a diagnosis which at this stage must always be uncertain. The appearance of any sign of organic spinal disease

in an anaemic patient, especially at or beyond middle age, should at once suggest the diagnosis, whether the spinal symptoms present consist in a slight spastic paraplegia, as is commonly the case, or in a loss of the deep reflexes which is a rare event. Where anaemia is not conspicuous and the signs of organic nervous change are distinct but as yet slight, the disease must be differentiated from the spinal form of disseminated sclerosis, since slight spastic ataxia is common to both diseases. Peripheral sensations and peripheral numbness are not features of disseminated sclerosis, whereas diplopia, nystagmus, transient amblyopia, sphincter trouble, and slight intention-tremor of the upper limbs are characteristic early symptoms of this malady, and do not form part of the symptomatology of subacute combined degeneration, with the exception of sphincter trouble which here only occurs as a relatively late symptom. In the rarer cases of subacute combined degeneration in which loss of knee-jerk is one of the earliest signs, distinction must be made from cases of early tabes dorsalis. The extensor response in the plantar reflex, which is almost invariable in subacute degeneration and which is very rare in early tabes, and the entirely different distribution of the sensory loss in the two diseases, should serve to prevent confusion. It may be pointed out also that lightning-pains and reflex iridoplegia, although they are not uncommon in combined degeneration, are late symptoms, whereas in tabes they are usually early symptoms. In this "tabetic" form of the disease anaemia has been conspicuous when the spinal symptoms have appeared. The diagnosis from disseminated sclerosis and tabes is further aided by the age-incidence of the disease; for although the age-incidences of the three diseases overlap, the greatest incidence of subacute combined degeneration is in the sixth decade of life, when disseminated sclerosis does not occur and the onset of tabes is rare.

In the well-developed stages of the disease its recognition presents no difficulty. Attention is quickly attracted to the peculiar nature of the disease by the conspicuous anaemia, which is rarely long delayed when the paraplegia becomes severe, the skin not infrequently assuming a striking lemon-yellow colour. Following a period of slight paraplegia, often lengthy, the steadily increasing paralysis of the lower extremities, with perhaps sudden exacerbations producing complete and lasting helplessness, the characteristic distribution of the sensory loss which spreads steadily upwards towards the cervical region, the severe lightning pains, the irregular pyrexia, the anaemia, and the relatively late onset of sphincter trouble serve to separate this disease from other forms of paraplegia. The change from the spastic to the flaccid type of paraplegia, with loss of the deep reflexes and persistence of the extensor response, which occurs in a majority of the cases during the late stages, is highly characteristic, and in a case seen for the first time in the flaccid state a history of preceding spasticity should suggest the correct diagnosis.

The diseases likely to be confused with subacute combined degeneration in its later stages are tabes, acute myelitis, polyneuritis, spinal tumour, and the various forms of postero-lateral sclerosis.

In the majority of cases the paraplegia is of the spastic type for the greater period of the course of the disease, and the resemblance to tabes ceases with the lightning pains and the occasional reflex iridoplegia. It is only in those cases which are flaccid from the first and in those that present a flaccid terminal stage that any doubt can arise. A history of spasticity changing to the flaccid state will distinguish the latter cases, and the severity of the paralysis, the intensity and peculiar distribution of the sensory loss, the rapid muscular wasting and lowering of faradic excitability, and that sure sign of involvement of the pyramidal tracts—the extensor response in the plantar reflex—will leave no difficulty in separating the two diseases.

In rare cases with a very rapid onset, and in cases with sudden and severe exacerbation of previously slight symptoms, the question of acute myelitis may arise. The course of the paraplegia of acute myelitis, at first complete and flaccid, and tending rapidly to become spastic and to improve, and the distribution of the anaesthesia in the two diseases, together with the presence or absence of any characteristic feature of combined degeneration, and especially of the anaemia, will serve to distinguish between the two conditions in the rare instances in which confusion is possible. The resemblance between combined degeneration and polyneuritis is but slight and superficial. It may be suggested by the peripheral sensations and the peripheral sensory loss. The symptoms of organic involvement of the spinal cord which are never absent in combined degeneration, such as spastic paraplegia, girdle sensations, sphincter involvement, and the extensor plantar response, render any confusion between the two conditions impossible.

A tumour implicating the spinal cord and giving rise first to slight and then to severe spastic paraplegia, and finally to flaccid paraplegia, may produce a clinical picture somewhat resembling that of a rapid case of subacute combined degeneration. The absence of severe pains preceding the paralysis, and the distribution of the physical signs in very unequal degree in the upper and lower extremities, the distribution and spread of the sensory loss, and the absence of the strict transverse limitation of the signs which is characteristic of a local spinal lesion, should prevent an error in diagnosis.

The distinction from the various diseases which are grouped together as postero-lateral sclerosis presents little difficulty. Burr and MacCarthy classify these diseases as follows:—(1) Friedreich's Disease, (2) tabes dorsalis with diffuse sclerosis, (3) tabes dorsalis with pyramidal degeneration, (4) amyotrophic lateral sclerosis with posterior sclerosis (5), primary lateral sclerosis (diplegia) with posterior sclerosis, (6) interstitial diffuse sclerosis of chronic alcoholism, and (7) systemic combined sclerosis. It is obvious that the symptomatology of most of these conditions departs so widely from that of the disease under consideration as to leave little possibility of confusion. The forms of tabes with pyramidal degeneration, however, require careful differentiation. The history of the illness, the peculiarity of the sensory disturbances, and especially the distribution of



the sensory loss in the two diseases, the presence or absence of anaemia, and the presence of such distinctive signs of tabes as crises, optic atrophy, or arthropathy, are the chief points to be relied upon.

It is conceivable that the coincidence of severe anaemia with any of the varieties of spinal paralysis in the same patient might give rise to difficulty and error in the diagnosis of this disease. This, however, seldom occurs, for on the one hand the type of the spinal paralysis in subacute combined degeneration is characteristic and is distinct from other forms of spinal paralysis, and on the other hand the anaemia may present characters both in nature and degree which are of diagnostic importance. For example, chlorosis in a young woman may coexist with the spinal form of disseminated sclerosis, but the distinction of this condition from combined degeneration is not difficult since the anaemia of the latter disease is never of the chlorotic type, and the paralysis in the two conditions usually shews distinctive peculiarities.

**Prognosis.**—There is no evidence that recovery from this disease occurs in any of its stages. The temporary improvements occasionally seen are improvements in the general health and in the anaemia rather than any lessening in the gravity of the nervous manifestations. It is not possible to make a precise prognosis as to the duration of life in any given case, but speaking generally the duration of the disease is inversely proportional to the rapidity of the onset and development of symptoms. The more severe the anaemia, the sooner may the fatal result be expected. Those patients in whom the spastic state persists survive longer than those who become flaccid.

**Treatment.**—No treatment has yet been found to influence the progressive course of the nervous manifestations in any way. A line of procedure that may possibly be successful is suggested by the hypothesis that some of the severe anaemias are due to chronic infections of the alimentary tract. It is possible that both the anaemia and the nervous symptoms of subacute combined degeneration may result from the absorption of a poison of this nature. Careful attention to any septic conditions of the mouth and of the pharynx, and to any form of gastro-enteritis that may be present, is therefore imperative. The isolation from the intestinal contents of organisms to which the bodily resistance is low and the administration of vaccins prepared from these organisms may prove useful. The use of intestinal antiseptics should never be omitted. The nourishment of the patient demands every attention. The administration of iron and especially of arsenic sometimes brings about remarkable temporary improvements in the anaemia. Arsenic may be given by the mouth, but hypodermic injection in the form of atoxyl or soamin is preferable. The amblyopia and blindness that occasionally result from the administration of these drugs should be borne in mind, and they should be at once discontinued if the slightest sign of visual disturbance appear. Any suppurative condition of the body should be energetically treated. Every care should be taken to delay the advent of bed-sores and of cystitis as long as possible. When present these are often amenable to

treatment in the earlier stages of the disease and in the less acute cases, but in the more acute cases and in the later stages they are inevitable, and the bodily vitality is too low for any reparative process to take place. Lightning pains and other pains are relieved by the various analgesic coal-tar derivatives, such as acetanilide, phenazone, ammonol. Reflex flexor spasms are among the most troublesome of the symptoms since their frequent occurrence denies sleep to the patient, and they are most important factors in the causation of bed-sores. The only remedy that seems to have a special influence in checking these spasms is veronal.

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## SENILE PARAPLEGIA

By PURVES STEWART, M.D., F.R.C.P.

OLD age is associated with a diminution in the activity of many bodily and mental functions. The anatomical and molecular changes of physiological senility constitute a wide and interesting study which has been fully dealt with elsewhere (Vol. I. p. 181). Amongst these changes, a certain degree of muscular enfeeblement is normal in advanced life. Sometimes, however, definite pathological changes are superadded, whereby the motor weakness is specially accentuated in the lower limbs so that the patient becomes more or less paraplegic. To this pathological feebleness the name senile paraplegia has been given. Various clinical forms are met with, according to the particular part of the motor apparatus primarily affected, whether the muscles, the peripheral nerves, the spinal cord, or the brain. The peripheral nerves are rarely attacked by paralytic affections in old age, so that practically we have to deal with three main forms of senile paraplegia: the muscular, the spinal, and the cerebral, which are really three separate diseases.

**Senile Paraplegia from Muscular Sclerosis and Contracture.**—In this disease the nervous system, central and peripheral, is essentially sound, but there occur in the muscles certain changes which gradually impair the patient's powers of walking.

The *etiology* of these muscular changes, why, for example, some old people are attacked whilst others escape, is quite obscure. The malady rarely develops before the age of seventy years, and in 6 out of 7 cases recently studied by Lejonne and Lhermitte the age of onset was over seventy-five. Old women appear to be more frequently attacked than old men. Neither senile dementia nor cachexia is a necessary antecedent. Nor is there any apparent causal connexion with the gouty or rheumatic diatheses.

*The morbid anatomy* of the disease is perfectly definite. There is abnormal hardness and contracture of certain muscles, especially of the flexors and adductors of the hips and flexors of the knees, most marked in the hamstring muscles. The whole of each affected muscle is diffusely permeated with fibrous tissue: the muscle-fibres are diminished in size, and, despite the general emaciation of the patient, there is fatty infiltration of the muscles, giving them a colour which even to the naked eye is paler than normal. On the other hand, the joints, hips, knees, and ankles are usually free from morbid changes. The peripheral nerves and central nervous system, apart from the arterial and other changes incidental to old age, do not shew any lesion of importance.

*The clinical course* of the disease is one of slowly-increasing weakness of the lower limbs, insidious in onset, and accompanied by gnawing or



cramp-like muscular pains, especially in the calves. Within a few months the patient becomes bedridden. The sensory functions, however, are normal; the deep and superficial reflexes are unaltered; and the sphincters remain intact. The muscles, which at the onset of the malady were flabby and soft, gradually become stiff and undergo contracture, and are painful if pressure or passive extension be attempted; but the nerve-trunks are not tender. The lower limbs gradually assume a position of extreme flexion and adduction of the hips, flexion of the knees, and extension of the ankles, so that ultimately the patient lies on his side in a characteristic attitude, with the hips and knees fully flexed, the heels being in contact with the buttocks. The joints themselves, hips, knees, and ankles, though apparently large by contrast with the wasted muscles, are free from true deformity, and although all their movements are extremely limited in range, no movements are impossible. There are no fibrillar tremors in the muscles, and the electrical reactions are normal. After lasting several years, the morbid process may spread to the muscles of the trunk, and even to the upper limbs, though these latter are never so severely affected as the lower extremities. Bed-sores do not occur. The disease is not fatal of itself; it may last from three years upwards. Death occurs from intercurrent complications or from simple feebleness.

The *diagnosis* as a rule does not present any difficulty. The absence of disturbances of sensation or of alteration in the reflexes, and the escape of the sphincters, distinguish it from spinal or cerebral paraplegia. The only conditions with which it may be confounded are those of chronic rheumatism or chronic osteo-arthritis. Passive movement of the joints, by shewing the absence of arthritic changes, suffices to distinguish it from true joint-disease. The disease, though not of itself fatal, tends to become progressively worse.

*Treatment*.—All that can be done is to endeavour to retard the progress of the disease and to alleviate the muscular pains. This is best accomplished by gentle massage and passive movements, together with occasional hot baths.

**Senile Paraplegia from Spinal Sclerosis.**—*Morbid Anatomy*.—There is an irregular diffuse sclerosis of the white matter of the spinal cord. The posterior columns, and still more the lateral columns, shew a sclerotic change which is essentially irregular—or “polyfascicular”—in distribution, to adopt the terminology of Lejonne and Lhermitte. The relation of the sclerosis to concomitant arteriosclerosis of the spinal vessels has been a matter of dispute. Whilst some observers (Demange, Pic and Bonna-mour) regard the spinal sclerosis as directly resulting from atheroma of the medullary vessels, the evidence of Lejonne and Lhermitte is to shew that the intensity of the spinal sclerosis is not in any way proportional to the degree of arterial change, and that the sclerosis is not necessarily perivascular in distribution. It is true that arteriosclerosis of medullary vessels may seriously impair the nutrition of the spinal cord, producing a slowly-progressive paraplegia; but the cases in which these changes have been demonstrated, notably by Hirsch and by Collins and Zabriskie,

have been in patients who could hardly be regarded as senile. Hirsch's cases varied in age from forty-four to sixty-five years, and Collins's patient was fifty-one years old. The sclerosis in the spinal form of senile paraplegia is not systemic in distribution; in other words, it is not limited to special tracts or paths in the cord. Thus, whilst the posterior columns are sclerosed more or less symmetrically, the lateral columns are often affected in an irregular fashion, the crossed pyramidal, the dorsal cerebellar, or the ventral cerebellar tracts being implicated indifferently. The extent of sclerosis also varies irregularly at different levels in the cord. The brain does not shew any constant abnormality in the form of sclerosis.

*Clinically* the disease has an insidious onset; there is gradual and progressive feebleness of the lower limbs, practically symmetrical on the two sides, together with dull pains of moderate severity in the limbs. The patient, whose psychical condition is unimpaired, and whose general nutrition as a rule remains good, manages to get about for two or three years or longer. The deep reflexes in the lower limbs are moderately increased, and the plantar reflexes may be extensor, though this is not constant. After several years of slowly-advancing rigidity of the legs, the spasticity and feebleness increase more rapidly, the changes in the reflexes become accentuated, and contractures appear which ultimately prevent the patient from walking and render him bedridden. These contractures at the hips, knees, and ankles are usually flexor in type; less commonly the hips are contracted in the flexed posture while the knees and ankles are extended. Sphincter troubles now supervene, and the patient becomes emaciated. Only towards the close does mental feebleness set in, and the appearance of bed-sores may hasten the fatal termination from exhaustion.

*Diagnosis.*—In distinguishing the spinal form of paraplegia from that of museular origin, the important points to note are the exaggeration of the deep reflexes and the presence in some cases of the extensor type of plantar reflex. To differentiate the disease from the cerebral form of senile paraplegia, the chief diagnostic points are the symmetry of the clinical phenomena, the slow course of the disease, and the fact that throughout the greater part of the malady the mental faculties remain intact.

*Treatment* can only be symptomatic. Assiduous nursing may prevent the appearance of the bed-sores which tend to usher in the final stage of the disease.

**Senile Paraplegia of Cerebral Origin.**—Several morbid processes in the senile brain are capable of provoking paraplegic symptoms; some cases of paralysis agitans, as Sir W. Gowers long ago emphasised, present such a degree of rigidity as to render progression very slow and difficult, and in the absence of tremors, a not infrequent event, the superficial observer may be misled. But the characteristic rigidity of paralysis agitans affects not only the limbs, but also the trunk and face, and together with the absence of disturbances of the reflexes, should render the diagnosis of paralysis agitans easy.

Genuine senile paraplegia, however, can be produced by cerebral lesions. In the first place and less commonly, there may be a chronic molecular degenerative process attacking the superficial layers of the cerebral cortex but not extending deeply enough to implicate the pyramidal cells, and therefore not producing any descending degeneration of the pyramidal tracts. Such cases have been recorded, and their morbid anatomy verified by Spielmeyer and others. The clinical phenomena are those of slowly-progressive weakness and spasticity of the limbs, more marked in the legs than in the arms, with increased deep jerks and extensor plantar reflexes, exactly as in true disease of the pyramidal tracts. A mild degree of dementia is also present, doubtless due to the same degenerative process attacking the higher psychical cortical centres. Spielmeyer proposes to name this form "intracerebral" diplegia, to distinguish it from the commoner type of diplegia due to degeneration of the pyramidal motor system. This intracerebral form cannot be differentiated clinically, with any degree of confidence, from the other form of senile paraplegia which will now be described.

The second type of senile paraplegia from cerebral disease is due to foci of "lacunar" softening, bilaterally but asymmetrically distributed in the neighbourhood of the basal ganglia and pyramidal paths. The lacunar hemiplegia of old age has been established by Marie, Ferrand, Catola and others as a clinical and pathological entity, and the morbid anatomy of senile lacunar paraplegia is somewhat similar. Examination of the brain shews numerous foci of perivascular disintegration, distributed asymmetrically in the basal ganglia of both sides, especially in the optic thalami and lenticular nuclei, sometimes, though less frequently, in the internal capsule itself. There is also descending degeneration of the crossed and direct pyramidal tracts in the cord, corresponding with the cerebral lacunae, that is to say, not absolutely symmetrical in intensity. There may be in addition a slight and irregular sclerosis of the posterior columns of the cord in the cervical and upper thoracic regions, but such posterior degenerations are not radicular in distribution, nor do the posterior roots shew any evidence of degeneration.

From these data it might perhaps be expected that this form of senile paraplegia would resemble an ordinary diplegia resulting from a second attack of lacunar hemiplegia on the opposite side from the first softening; this, however, is not the case. Unlike lacunar hemiplegia, which usually comes on suddenly though without loss of consciousness, and presents definite hemiplegic symptoms, though slight in degree, lacunar paraplegia usually has an insidious onset without an initial stroke of hemiplegia or hemiparesis. The patient begins to notice undue fatigue of the legs, which tend to drag as he walks; his gait becomes feeble and shuffling, and ultimately he cannot walk at all. The deep jerks are increased, ankle-clonus is rare, but the plantar reflexes are often extensor in type. There is no sphincter trouble, and contractures, if present, are but slight in degree, thereby contrasting both with the muscular and with the spinal forms already described. Mental enfeeblement rapidly ensues, doubtless



due to the occurrence of other lacunar softenings. When this stage is reached, the sphincters become neglected and bed-sores are apt to appear, hastening the fatal termination.

The cerebral form of senile paraplegia is even less amenable to *treatment* than the other varieties. In view of our helplessness to cope with the occurrence of lacunar softenings or to remedy them, treatment must be entirely symptomatic and confined to the alleviation of intercurrent symptoms.

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P. S.

#### DISSEMINATED SCLEROSIS

SYNONYMS.—*Multiple Sclerosis* ; *Insular Sclerosis* ; *Sclérose en plaques* ; *Zerstreute Sklerose* ; *Herdsklerose* ; *Polynestic Sclerosis*

By J. S. RISIEN RUSSELL, M.D., F.R.C.P.

DISSEMINATED sclerosis is a disease of the brain, spinal cord, and, it may be, peripheral nerves ; characterised by areas of sclerosis of varying sizes, distributed at random, and destroying and replacing the nerve elements.

**History.**—The first record of this curious disease is in the drawings by Cruveilhier in his *Anatomie Pathologique*, published between 1835 and 1842. The condition is depicted as it was seen in the pons, medulla, and spinal cord in four patients, and was called "grey degeneration." Carswell's *Illustrations of the Elementary Forms of Disease*, published in 1838, also contains pictorial representations of the morbid appearances. The first clinical study of the disease was made by Frerichs in 1849, and some of his cases were subsequently examined after death by Valentin, in 1856. It was not until six years after this that the condition was made the subject of careful study at the Salpêtrière, when Charcot, working under Vulpian, took the chief part in the investigations, and, in

1866, published a lecture on the subject which made the disease widely known. This production of the great French neurologist still remains a faithful picture of the classical type of the clinical manifestations of the disease; although we have since learnt that other types, equally characteristic but differing widely from that originally described, may be constructed. In the interval between the appearance of the publications of Frerichs and Valentiner on the one hand, and that of Charcot on the other, Turek studied the disease in its physiological bearings, Rokitansky and Rindfleisch did much to advance the study of its morbid anatomy, and Bärwinkel pointed out that the tremor was evoked on voluntary movement only. After Charcot's publication, Leo and others studied the disease in Germany; but it was not until 1873 that any attention was given to the subject in this country, when Moxon recorded a case. Two years later the same observer published a paper dealing with 8 cases.

**Etiology.**—The cause of disseminated sclerosis is still shrouded in great obscurity, but much valuable information bearing on the subject has accumulated during recent years.

**Geographical Distribution.**—The question whether this disease is more common in some countries than in others has engaged the attention of several observers, and Dr. Byrom Bramwell has pointed out that the disease does not appear to be nearly so common in America as in this country. E. W. Taylor, however, has since adduced evidence to shew that the disease is not so rare in America as previous records would suggest, and probably there is a good deal of justification for his contention that the diagnosis is not made as often as it should be, because the majority of American physicians are not sufficiently familiar with the aberrant types of the disease.

**Heredity.**—It is only exceptionally that any direct heredity has been traced, or that more than one member of the same family has been affected in the way that obtained in Reynolds's cases. A striking instance of the kind has been recorded by Eichhorst, in which a mother and her son, aged eight years, were both the subjects of this disease; the author was able in both cases to verify his diagnosis by necropsy. More commonly an indirect neuropathic inheritance can be established in the way of some other chronic disease of the nervous system, such as paralysis of some kind, epilepsy, or insanity.

**Age.**—Most commonly the symptoms appear in early adult life. Marie, who regards this as important in diagnosis, states that most cases occur between the ages of twenty and thirty. It is supposed that the disease may occur in childhood, though Strümpell doubts the genuineness of most of such recorded cases, and I have never met with a case of the kind. Meyer collected 19 cases in 1887, Totzke collected 34, and according to Pritchard more than 50 cases have been reported. Of 31 of Totzke's cases, in 2 the symptoms appear to have been present at birth; Ross stated indeed that the disease might affect children at the breast. In 19 of Totzke's cases the symptoms were observed before the

age of six years, and in 12 between the ages of six and fourteen years. As the clinical course of the disease is, as a rule, protracted, it is not surprising that the opportunities of necropsy in children have been few. The 3 cases with necropsies recorded by Zenker, Schüle, and Pollák, and regarded by earlier writers as proving that disseminated sclerosis occurs in children, were not instances of this disease at all. Its occurrence in childhood has, however, been said to be established by competent observers, and it is stated that cases have been met with in adults in which it has been possible to trace the origin of the disease to childhood. If it is true that the affection may be met with in young babies, this naturally suggests the possibility of a congenital factor in its etiology. Of this we have no other evidence except that supplied by the morbid appearances met with, which have been likened by some observers to the gliomatosis found in cases of syringomyelia, and which have accordingly suggested that the starting-point of the morbid process is some congenital imperfection in the development of the neuroglial tissue. Two cases alluded to by Strümpell, in which disseminated sclerosis was accompanied by central gliosis and hydromyelia, are further suggestive in this connexion.

It is rare for the disease to appear for the first time after the age of forty or forty-five; though its occurrence at sixty is recorded.

*Sex.*—The affection is as frequent in one sex as in the other; the statistics of some authors suggest a preponderance in females, of others a preponderance in males. In 33 instances collected by Charcot, 24 females were affected and only 9 males. Ross, again, was of opinion that girls are more frequently affected than boys. The reverse, however, obtains in 29 cases recorded by Blumreich and Jacoby, 23 of which were male and 6 female; of 58 cases collected by Probst, 34 were men and 24 women, and in the statistics of Marie, Kraft-Ebing, and Redlich, more men were affected than women.

*Occupation.*—Oppenheim has insisted that persons engaged in certain trades are liable to become the subjects of this disease. In all such cases some toxic agent is held responsible, notably some metallic poison.

*Intoxications.*—A toxic agent was traced in 11 out of 28 cases by Oppenheim, who found lead the most common, though copper, zinc, and other metallic poisons were proved in some of the cases. On the other hand, the clinical picture of disseminated sclerosis may be present during life but the characteristic lesions be wanting on necropsy; as in a patient of Oppenheim's, who suffered repeatedly from lead poisoning, and in whom combined system degeneration was found after death. Important as may be the immediate or remote influence of such toxic agents in certain cases, yet when we consider how many people are exempt from them, and who nevertheless become the subjects of disseminated sclerosis, we are forced to the conclusion that there must be some more general etiological factor, about which at present we know but little. Alcohol has also been supposed to account for some cases.



*Infectious Diseases.*—Closely allied to the cases just considered are those which occur after one or other of the infectious fevers. Bruns considers that it may follow any infectious disease, and Charcot met with it after enteric fever, cholera, and small-pox. Kahler and others have regarded scarlet fever as especially apt to be attended with this result; and Marie found that there had been enteric fever in 11 out of 25 cases in which there was a history of infectious diseases. Many other diseases have, more rarely, been the preeursors of this affection—notably malaria, influenza, pneumonia, measles, diphtheria, whooping-cough, erysipelas, and dysentery; and Probst has found articular rheumatism an antecedent. With regard to malaria much caution is needed, for in marked contrast to true disseminated sclerosis, the tendency of these cases has been to result in recovery. Cases of the kind have been recorded by Torti and Angelini, Bastianelli, Camellis and Boinet, and Salebert; and the two first-named have regarded the symptoms as the result of an intoxication of the nerve-centres. Caution is also needed in ascribing disseminated sclerosis to a disease so prevalent as influenza, for the association may be accidental, although the patient is made worse owing to the debility resulting from influenza. Strümpell does not regard the infectious hypothesis as admissible, for he failed in 24 consecutive cases to establish any such connexion, whilst Krafft-Ebing could only do so in 6 cases out of 53.

*Syphilis.*—There are few diseases of the nervous system in which syphilis can be excluded as a cause more surely, and yet some consider it a causal factor (Michailow, Jacobsohn, Moneorvo). Carrier agrees with Moneorvo that hereditary syphilis is an important cause of disseminated sclerosis in young children.

*Pregnancy.*—Pregnancy and parturition have a deleterious effect, as observed by Sir W. Gowers, and are responsible for relapses or more rapid progress of the disease, whilst it not infrequently happens that the first symptoms of the malady are noticed during pregnancy or after parturition.

*Antecedent Affections of the Nervous System.*—Some form of myelitis, either primary or following an injury, has been most commonly met with in this association, but as disseminated sclerosis may begin in a way that simulates acute myelitis, the association that has been claimed is open to question. According to von Leyden, cases may begin like an acute myelitis and go on to sclerosis. Disseminated sclerosis may be found after death in cases in which, many years before, some acute illness had been followed by disseminated myelitis.

*Trauma* appears to play some part in producing the disease; but whether a fall or blow is alone capable of generating such a process, or whether it is only the means of lighting into activity some dormant pre-existing morbid condition, congenital or otherwise, must remain for future research to determine. Mendel has more especially insisted that the disease may be caused by injury; Blumreich and Jacoby established a history of injury in 11 of their 29 cases; Hoffmann in 11 per cent of

his cases, and Bruns has met with an instance of the kind which began with optic neuritis.

*Cold.*—Exposure to cold or chill has preceded the occurrence of a good many cases; thus, in a case observed by Bärwinkel, the patient fell into water and allowed his clothes to dry on him; three days later symptoms of disseminated sclerosis appeared. Some reserve is needed in accepting such cases—as careful inquiry will sometimes elicit evidence that the disease existed before the wetting or exposure; though the symptoms had not been sufficient to arrest the patient's attention. In no fewer than 40 out of his 53 cases, however, Kraft-Ebing obtained a history of severe chill as an antecedent; and Probst concludes that chill is the most common cause.

*Fatigue.*—What has just been said with regard to wet and cold applies equally to fatigue; the probabilities being that where over-exertion has appeared responsible for the disease, the true explanation was, that the fatigue merely accentuated or evoked phenomena previously existing, though more or less dormant.

*Emotion.*—It is difficult to see how emotional influences can play any part in the generation of an affection like disseminated sclerosis, in which such pronounced structural alterations occur in the nervous system; nevertheless, the association occurs; as in a case in which the symptoms of disseminated sclerosis appeared suddenly a few days after a severe mental shock (Jordan). Probably the explanation suggested for the cases following chill, fatigue, or injury, is equally true here; and certainly any of these factors seem adequate to determine relapses, or to accelerate the morbid condition otherwise originated.

*Morbid Anatomy.*—The patches of sclerosis are irregularly distributed throughout the nervous system in the most random manner possible; there being no part which is not liable to be so affected, though some parts appear to be especially prone to invasion. That the disease is a general one, at any rate so far as the central nervous system is concerned, there can be no question; and, accordingly, the view formerly held that a cerebral as distinguished from a spinal form of the affection can be recognised pathologically as well as clinically is no longer tenable. Although the clinical manifestations of the disease may point to the brain or spinal cord being separately affected, it is highly improbable that a careful examination of the nervous system after death, macroscopically and microscopically, will fail to reveal unequivocal evidences of affection of all parts of the central nervous system at least, whether any concomitant affection of the peripheral nervous system be present or not. Of the apparently isolated affections of a particular region of the nervous system, the spinal form is the more frequent; patches of sclerosis in the brain, too small to give rise to symptoms, may therefore readily be overlooked after death, unless great care be exercised in the examination. On the other hand, in rare instances in which the symptoms point to affection of the brain alone, little difficulty can be experienced in detecting evidences of concomitant affection of the spinal cord; that is, if

proper opportunity is found for the study of the morbid anatomy of the case. Charcot, while recognising a pure spinal form of the affection, admitted that in the cerebral form the possibility that areas of sclerosis also exist in the spinal cord could not be excluded; and Erb believes that a purely cerebral or spinal form of the disease is very rare. An exception to the rule appears to be forthcoming in a case of disseminated sclerosis, published by Probst, in which, with patches of sclerosis in the pons and medulla, there existed no such sclerotic areas in the spinal cord: there was, however, a systemic degeneration of the crossed and direct pyramidal tracts; the pyramidal fibres, from the proximal end of the pons to the lumbar region of the spinal cord, being degenerated. There was also a less pronounced degeneration of the postero-internal columns, extending from the upper part of the thoracic region of the cord to the termination of the tracts in the nucleus of the funiculus gracilis on each side. As I have said, although in so far as the nervous system is concerned the disease is a general one, it appears, nevertheless, to be more prone to invade certain regions than others. If, in the first place, it appears to affect the central nervous system, as opposed to the peripheral, more commonly and in greater degree, we must remember that even this statement, based, as it is, on past observations, is one which may have to be considerably modified in the light of future researches; for the peripheral nervous system in cases of disseminated sclerosis has not been examined with the same regularity and care that has been bestowed upon the central nervous system.

Most observers have recognised certain *seats of election* in the disease. According to Sir W. Gowers, the centrum ovale of the cerebral hemispheres is a frequent seat, whereas few patches occur in the cerebellum. Erb finds the floor of the fourth ventricle, the pons, the walls of the lateral ventricles, the white substance of the cerebral hemispheres, and the white tracts of the spinal cord, to be the parts most commonly affected. Strümpell is of opinion that the patches of sclerosis occur specially in the white substance of the hemispheres, the walls of the lateral ventricles, and the corpus callosum; that they are somewhat plentiful in the pons; less so in the medulla; but very plentiful in the spinal cord, especially in its white substance. My own observations are in harmony with those of Strümpell, which differ little from those of Erb. The former observer's statement, however, that the medulla is usually less affected than the pons and spinal cord, does not accord with what I have found in the cases that I have examined. I can corroborate the statements of those observers, including Sir W. Gowers, who have found that, as a rule, few patches occur in the cerebellum; but my observations do not accord with those of Obersteiner, who finds that patches of sclerosis occur less commonly in the lumbar region of the spinal cord than at higher levels.

A further point of importance, with regard to the distribution of the sclerotic areas, is the degree in which the white matter is affected as compared with the grey. Since the time of Charcot, who was of opinion



that the patches are rarely found in the cortex of the brain or cerebellum, most observers have expressed similar views. Sir W. Gowers believes that the patches seldom invade the grey matter of the cortex, and that they never appear to begin in it. It is very striking, sometimes, to see how strictly limited the patches are to the white matter, at any rate as seen macroscopically, abutting on the surface grey matter, both in the cerebrum and in the cerebellum, without actually invading it; but that in other instances the grey matter of the cortex is invaded there can be no question. E. W. Taylor finds no justification for the view that, in respect of the general distribution of the disease, there is any seat of election; he finds not only that the grey matter of the cortex of the cerebrum and cerebellum does not escape, but also that the patches may begin in the cortical grey matter, and be limited to it. This latter point I have not myself had an opportunity of observing; and, while fully agreeing with Taylor that the grey matter of the cerebrum and cerebellum does not escape, my observations certainly support the views of those who regard these parts as being less commonly affected than the white matter. A curious and interesting point, one on which others also have commented, is that, in spite of this slighter tendency to affection of the surface grey matter of the cerebral hemispheres, the grey matter of the basal ganglia appears to be a favourite seat for the sclerotic process.

There seems to be no rule as regards the frequency of affection of the grey and white matter of the crus, pons, and medulla oblongata; and the view that the ventral aspect of the pons is more commonly affected than the dorsal is not supported by my observations. The cases I have examined shew an irregular, random distribution in the crus, pons, and medulla, with no respect for grey matter as opposed to white; indeed, in so far as these observations go, the grey matter and mixed regions were possibly more affected than the purely white matter of the ventral aspect of these parts of the central nervous system. Buchwald and others thought that certain systems in the spinal cord are specially prone to participate; and Bourneville and Guérard noted a predominance of the patches in the symmetrical columns of the cord. However true these statements may be, the most varied pictures may be seen in the spinal cord as a result of the distribution of the sclerotic areas. I have seen a practically complete transverse lesion produced by a patch of sclerosis; an exceedingly small group of myelinated fibres alone remaining in one part of the periphery of the transverse section: in other instances an almost accurate hemisection had been similarly produced; in others but a quadrant of the sectional area had been involved, whilst in others several patches were scattered indifferently through the transverse section. As far then as my observations go, they certainly accord with those of others who have found the patches of sclerosis most commonly affecting the white matter of the cord; but the grey matter by no means escapes, for patches of sclerosis may be found not only invading it, but, in certain regions, practically limited to it.

The degree to which *the peripheral nervous system* is affected in dis-

seminated sclerosis is a question that has received comparatively scant attention; so that, beyond certain facts in connexion with the cranial nerves and the spinal nerve-roots, we have very little definite information to guide us. Nearly all authors have noted affection of some of the cranial nerves. Bourneville and Guérard, while citing the observations of Cruveilhier, Skoda, Vulpian, Liouville, and Ordenstein—who found patches of sclerosis in the hypoglossal, vagus, glossopharyngeal, optic, olfactory, and oculomotor nerves—believed that the cranial nerves generally escape. Jolly also found the cranial nerves unaffected; whilst Charcot was of opinion that the optic, olfactory, and fifth cranial nerves alone are affected. E. W. Taylor found participation of all the cranial nerves (with the exception of the olfactory, which was not examined) in two of his cases; either the nuclei, the central portion of the nerve from the nucleus to the surface of the pons or medulla, or some part of its peripheral course being diseased. In a third case he found the degeneration not so pronounced, but the roots or nuclei of most of the nerves were affected. Claus found the third, fourth, fifth, and twelfth cranial nerves most affected, the seventh and eighth but slightly so, and the olfactory and optic nerves free from change. Similar escape of the olfactory and optic nerves, which are usually regarded as favourite seats of the morbid process, has been noted by Probst, who found the facial, vagus, hypoglossal, and motor part of the fifth cranial nerves affected. Uthoff finds that some of the patches in the optic nerves are indistinguishable from those of a tabetic atrophy; otherwise the process is of an interstitial neuritic character. In all the cases examined by E. W. Taylor the optic chiasma was the seat of patches of sclerosis; and in two of them so pronounced was the change that scarcely any myelinated fibres were to be seen. Of two well-marked cases which I examined, the optic chiasma of one, while presenting patches of sclerosis, had much of its structure preserved; yet the optic tracts behind and the nerves in front were much more extensively destroyed: in the second case the chiasma and tracts were intact, and the peripheral portion of each nerve for a short distance behind the globe was affected; although a portion of the nerve next to the normal part did not contain any myelinated fibres, a few such fibres were to be seen in the portion of the nerve immediately behind the globe.

Charcot, Erb, E. W. Taylor, Probst, and others have noticed that *the spinal nerve-roots*, both motor and sensory, may be attacked; and Taylor in his cases found also an extensive degeneration of the nerves of the cauda equina.

*The appearance of the islets of sclerosis* is very characteristic, and, it appears to me, quite unlike that of any other morbid process in the nervous system. The patches are of a warm grey colour, or of a brownish- or reddish-grey; they are both darker and more translucent than the grey matter of the cerebral cortex. Sometimes they have quite a gelatinous appearance, and are more or less of this consistence on palpation, being distinctly soft; in other instances the patches, though

somewhat glistening, are firm in consistence. The sclerotic areas are irregular in outline, and to the naked eye appear sharply delimited from the adjacent healthy nervous tissue; they vary in size from areas a few millimetres in diameter to others whose diameter may be measured in centimetres rather than millimetres. When seen on the external surface of some part of the central nervous system, such as the pons, they may be on a level with the surrounding tissues, or may be slightly more prominent; whilst as seen on section of some part they are usually on the same level as the immediate surrounding tissues, or are, it may be, slightly depressed below that level. They are to be seen both on the external surface of the spinal cord and on section, and are usually greater in vertical than in transverse extent.

The *microscopical examination of affected parts* of the central nervous system may quite corroborate the impression gained on macroscopical examination in regard to the definite limitation of the affected areas from the surrounding healthy tissues. Charcot was of opinion that an intermediate zone of slighter affection separates the healthy from the diseased parts; and, although this is true of some patches, my observations quite accord with those of E. W. Taylor, who found, in the case of other patches, an abrupt transition from diseased to healthy tissue, without interposition of any zones of intermediate degrees. In my experience, even in the majority of instances in which an intermediate zone exists, the transition from normal to abnormal, in the sense of complete absence of myelinated fibres, is very rapid. There is one point at least with regard to the histological changes on which there is unanimity of opinion, all observers are agreed that the nerve-fibres in the affected areas are deprived of their *myelinated sheaths*.

Where transitional stages of the destructive process are met with, the nerve-fibres, instead of being completely denuded of their myelin sheaths, present various degrees of alteration of the same; the sheath may be swollen more or less uniformly, or in an irregular manner; knobby swellings of it may alone remain attached to the axis-cylinders in parts; or there may be no evidences of acute destruction of the myelin sheath, but rather an atrophy of it, a narrow ring only of myelin remaining around the axis-cylinder. Here and there granular cells and corpora amylacea may sometimes be seen.

The degree of resistance which the *axis-cylinders* offer to the destructive process is a curious feature of the disease. This has been insisted on by various writers who have dealt with the subject from the time of Charcot to the present day, but has been contradicted by Dr. Tredgold. Areas in which there is a complete absence of myelinated fibres may, nevertheless, be occupied by naked axis-cylinders, apparently unaltered in character. This, however, does not always obtain; for the axis-cylinders, though capable of resisting the destructive process, may in the end succumb like the other parts of the nerve elements. Popoff has brought forward evidence to support his contention that there is not in reality this supposed escape of the axis-cylinder in the destructive



process of the nerve elements; but that, having been destroyed, they are capable of regeneration, and that it is to this capacity that the naked axis-cylinders owe their presence. One of the facts on which Popoff places most reliance is that, according to him, the ends of many of the axis-cylinders may be seen to be composed of a bunch of fibrils, just as is seen in the process of regeneration of peripheral nerves; but there has been nothing in the appearances in the cases I have examined to lead me to any such conclusion, and Weigert, whose observations are based on his selective neuroglia stain, concluded that Popoff's supposed regenerated axis-cylinders are neuroglial fibrils.

The preservation of the axis-cylinders, in great degree at any rate, in disseminated sclerosis leads us next to consider what is perhaps the most extraordinary feature of the disease, certainly the most difficult of explanation; namely, that it is exceedingly rare to meet with any evidences of secondary degeneration of the nerve elements; and that when any such evidences are found, they are limited, as a rule, to a very small extent in the immediate neighbourhood of a sclerotic area. On examining, for instance, some of the affected parts of the spinal cord in which the morbid process has invaded one or other of the long systemic tracts, it seems incredible that no secondary degeneration of the fibres of the tract is to be found in regions remote from the sclerosed area; nevertheless, such is the case. The most reasonable explanation that has been offered for this absence of secondary degeneration of the nerve elements is that first suggested by Schultze, who attributed it to the preservation of the axis-cylinders, supposing that secondary degeneration only results when these are destroyed. Reasonable as this explanation is, it is not altogether satisfactory; for most observers are agreed that in the later stages of the morbid process destruction of the axis-cylinders does result; and this, it may be, in no mean proportion: yet even in such cases no secondary degeneration may be forthcoming. To explain this discrepancy, it has been urged that the destruction of the axis-cylinders does not take place in sufficient number to allow of the secondary degeneration being recognised—an argument which, while possibly justified where observations are based on the Weigert-Pal method of staining, cannot be regarded as satisfactory in so far as the Marchi method is concerned; for by the latter method isolated degenerated fibres can be picked out, and the presence of a collection of them is not required for the detection of the degeneration. Popoff's hypothesis with regard to regeneration of the axis-cylinders does not help us; as before regenerating they must be destroyed, and with their destruction we ought to find evidence of secondary degeneration, whether they are subsequently renewed or not. Yet there are very few recorded cases in which secondary degeneration has been established with certainty. Among those who have observed such degeneration are Jolly, Werdnig, Babinski, Redlich, and Rossolimo; but in cases of the kind the secondary degeneration has usually been traced but a very short distance from the sclerosed area. Buss found descending degeneration through the whole

lumbar cord, and an ascending degeneration of Goll's column and the direct cerebellar tract from the level of the eighth cervical nerve-roots to the medulla oblongata; but such a state of things must be exceptionally rare. The case recorded by Probst, and already referred to, is remarkable in that, with areas of sclerosis in the pons and medulla and none in the spinal cord, there was not only degeneration of the pyramidal tracts, but also of the postero-internal columns in the upper part of the cord. Another notable feature in the case is that, in spite of other tracts in the pons and medulla being affected as much as or even more than the pyramids, these fibres alone shewed signs of secondary degeneration. This case, however, seems open to the interpretation that two independent diseases existed in the same patient; though Probst considers this not to be so. Most observers have found either no secondary degeneration at all, or degeneration limited to a very short distance from the sclerotic areas. I have seen sclerosis so situated in system tracts as to be mistaken for a tract degeneration by those not sufficiently familiar with such appearances to be able to judge of their real significance; so that only the results of experienced observers can be relied on with any degree of confidence in this matter. Dr. Tredgold, however, considers that the view that ascending and descending degenerations do not occur is a fallacy, and he contends that the axis-cylinders do degenerate in the disease, whether owing to attack by the same morbid process or because they are unable to exist when deprived of their myelin sheaths he is unable to say.

Like the axis-cylinder, that portion of the neuron which comprises *the cell* is also unaffected till late in the course of the disease. Most authors state that such late affection of the ganglion-cells does take place; but Koppen, Rossolimo, and others have found these cells normal. It is surprising how much sclerosis may be found in the immediate neighbourhood of such cells without the cell itself shewing changes, even when examined by more recent and delicate methods. On the other hand, that the cells are destroyed when the sclerosis is most intense in the grey matter appears to me beyond question. Charcot and Bourneville, and Guérard all described a yellow degeneration of the cells; Sir. W. Gowers speaks of them as undergoing atrophy in the neighbourhood of sclerotic tissue; and Obersteiner considers that all the changes met with in the cells in myelitis may be present in this condition. Frommann, Schuster, and Bielschowsky have also noted cell changes. E. W. Taylor, while fully recognising that pigmentation of cells may have no pathological significance, more especially in old persons, considers that, taking into consideration the age of his patients and the degree of pigmentation met with in two of the most advanced cases, the condition must in them be regarded as pathological, a view supported by Dr. Tredgold. But for the preface to Taylor's observations, one would take any such results with considerable scepticism; as pronounced pigmentation of ganglion-cells may be met with where it clearly has no pathological significance. The necessity for caution is

further suggested by the fact that neither the axons nor dendrons of such cells shewed any evidences of degenerative changes in his cases. Apart from this widespread change in the cells, however, Taylor states that he found cells without nuclei in various stages of degeneration; and that, while the nerve-cells of the nuclei of the cranial nerves were mostly fully preserved, he established with certainty a diminution in the number of cells in the oculomotor nucleus, especially on one side. In one case he found that the cells were preserved in areas of the cerebral cortex where sclerosis was present, but that where the sclerosis was very advanced distinct atrophy with diminution in the number of cells appeared. In his third case, in which the sclerotic process was not so advanced, no distinct cell changes were found, excepting in a single group of ventral horn cells in the cervical region of the spinal cord. Taylor, therefore, concludes that degeneration of the ganglion-cells occurs, but only in an advanced stage of the process; for a long time they remain intact, and for the most part active, a fact that explains well why in disseminated sclerosis muscular atrophy and the reaction of degeneration are rare. In Probst's case the hypoglossal, vagus, facial, and trigeminal nuclei were affected by sclerotic patches, so that the interstitial tissue compressed and destroyed the nerve-cells; whilst, in the absence of any sclerotic areas in the spinal cord, such changes as were seen in the ventral horn cells were regarded as comparable with the changes which are met with in these cells secondarily to cerebral lesions.

Marked increase of the *interstitial tissue* has been described by nearly all observers as forming part of the anatomical picture. A case recorded by Reinhold was quite exceptional in this respect, in that there was extensive disappearance of the nerve-sheaths and axis-cylinders without increase of the glial tissue, except in the centre of the patches where there was slight hyperplasia. As a rule there is marked proliferation of the interstitial tissue, the dense mass of fibrils being arranged longitudinally where the patches occur in association with any of the long tracts of the central nervous system; many small glial cells are also seen, forming a feltwork of interlacing fibrils when some part of the grey matter is affected. In the latter case, instead of the fibrils being arranged parallel to the nerve-fibres, they spread out in all directions from a centre where the tissue is most dense; and they may be seen insinuating themselves between the nerve-elements at the periphery of the patches where the fibrillar meshwork is less dense; this change being accompanied by the presence of innumerable glial cells. Sometimes patches of increase of interstitial tissue are to be seen on the surface, and the pia may be adherent in such places; but there is nothing in these changes to support a view, formerly held, that the whole morbid process in this disease originates in the pia. The majority of the patches of sclerosis have no connexion whatever with the pia, and can in no sense be regarded as depending on any morbid process engendered in this membrane. Moreover, the slight changes which may sometimes be seen in the pia connected with a patch of surface



sclerosis are clearly secondary to the change in the cord, or other part of the nervous system concerned. Apart from such areas, the pia does not shew any evidence of alteration in structure. Some observers have described a round-celled proliferation as the earliest stage of the interstitial hyperplasia, such cells being described as especially plentiful in the neighbourhood of blood-vessels. Thus, Oppenheim found the vessels within the foci considerably increased and a diffuse infiltration of cellular elements around them, the majority of which were true plasma-cells, and are regarded as an expression of a more or less chronic inflammatory process. At some points there were numerous large polynuclear cells with many processes, assumed to be glial cells, and between them epithelioid cells (Friedmann's). Rindfleisch, Leubuscher, von Leyden, and Chvostek noted proliferation of the cells in the neuroglia. Chvostek and Ribbert held that the leucocytes wander out of the vessels and then become changed into fixed cells. Fürster also held that wandering leucocytes might become transformed into glial cells; so that originally wandering leucocytes were supposed to become fixed cells of connective-tissue type, which subsequently develop into fibrils. In the morbid patches it is difficult to be certain how far glial fibres and glial cells are related to each other; in all probability, however, glial fibres spring from the cells. The precise appearances met with depend on the ages of the patches: thus, in early patches little fibrillar structure is to be made out, the very fine fibre network being scarcely visible, and the chief change being a cell increase; in older patches the glial cells are more separated from each other, and the network of fibres is better seen. The oldest patches may have quite a homogeneous appearance; and in such patches Probst found, in addition to the small glial cells, larger spider-cells (14 to 20  $\mu$ ) with large nuclei; their processes forming a beautiful meshwork, the interspaces of which were homogeneous, with no ground substance to be seen; this description has been corroborated by Frommann, Hüber, and Redlich.

Whilst changes occur in connexion with the *blood-vessels* in a certain proportion of cases of disseminated sclerosis, such changes are not constant; some cases are normal in this respect. The vessel-walls may be thickened to a variable degree; in some cases the increase in thickness is slight, in others pronounced; but nuclear proliferation is usually slight. Moreover, the vessels are sometimes engorged, and there may be marked increase of the number of the smaller vessels, especially of the capillaries. In such cases leucocytes may escape from the vessels into the surrounding tissues, or small extravasations of blood are visible. The perivascular spaces are widened in many cases in which vascular changes are met with. Rindfleisch first described affection of the vessels in disseminated sclerosis, and a great many observers have since met with similar changes; but others (Leyden, Jolly, Buchwald, Hüber, and E. W. Taylor) have been unable to find any alteration in the vessels. In a case recorded by Probst, though there were no changes in the vessel-walls, there was engorgement of the capillaries and increase of them in places, with widening

of the perivascular space—conditions which have also been described by Leo, Kelp, Buchwald, Putzar, and others. Charcot, Guérard, and Frommann are among those who have found vascular changes; and, in addition to the more commonly described changes, they met with narrowing of the vessels. Ribbert, another author who has described changes in the vessels, found thrombus formations. Most observers have described thickening of the vessel-walls, widening of the perivascular lymph-space with a large number of leucocytes, and increase of nuclei of the vessel-walls.

**Pathology.**—Leaving out of consideration those points in the pathogeny of the disease already sufficiently dealt with in discussing its causes, we have still to consider the origin of the morbid process. Various views have been advanced on this subject, and cogent arguments have been used in support of this or that hypothesis. The first questions are whether the morbid process is one which affects the nerve-elements primarily, or whether the interstitial tissue suffers first? The explanation formerly accepted was that the process is primarily interstitial, consisting in a chronic inflammation; and that the myelin sheaths of the neurons suffer secondarily—a view that has been supported by Charcot, Erb, Gowers, Leyden, Wernicke, and others, but which is negatived by Dr. Tredgold. Leyden has gone even farther in this direction, and has contended that a multiple sclerosis may be evolved from an acute myelitis; moreover, in their article in Nothnagel's *Encyclopaedia of Medicine*, this observer and Goldscheider have treated disseminated sclerosis as a form of chronic myelitis. Bikeles also classes this disease as a myelitis.

The opposite view, which regards the disease as a primary affection of the myelin sheaths of the neurons with secondary hyperplasia of the interstitial tissues, owes its origin to Adamkiewicz, whose conclusions were, however, based on untrustworthy data. A case, recorded by Reinhold, and already cited, may be interpreted on the lines of Adamkiewicz's view. The anatomical changes were quite unusual; as has already been said, in the presence of extensive disappearance of the myelin sheaths and axis-cylinders there was little or no increase of the glial tissue; and Reinhold regarded the case as an early one of ischaemic or toxic degeneration, with much less of an inflammatory character. Hüber supports the view that the nerve-elements suffer primarily, and that the sclerosis is secondary to the affection of the parenchyma. He considers that there is a simple degenerative destruction of the myelin sheath or of the whole nerve-fibre, and that the process is not inflammatory as we are accustomed to see inflammation in acute myelitis, and Oppenheim points to the comparative integrity of the individual nervous constituents within the foci as distinguishing them from disseminated focal myelitis. Redlich holds similar views to those of Hüber, and they both could detect fresh patches where there was disappearance of the nerve-fibres in great masses without change anywhere in neighbouring interstitial tissue. Borst, F. Schob, and others similarly regard the glial proliferation as secondary, and the primary lesion as exogenous in origin

and as affecting the true nervous tissues, notably the medullary sheaths. Hüber's view has much to recommend it; moreover, a point which has oftentimes been suggested to me by a study of the morbid anatomy of this disease has not escaped his attention; namely, that an interstitial proliferation, originated by a parenchymatous degeneration, may spread beyond the limits of the nerve-elements primarily diseased, and may thus lead to secondary destruction of the nerve-elements of contiguous parts. In this way the fact may possibly be explained that in the outlying districts of a patch of sclerosis the interstitial tissue change is often obviously in advance of the destructive process in the nerve-elements. The importance of giving due consideration to this possibility will be obvious when it is remembered that this very fact, that in the peripheral zones of sclerotic areas the interstitial process may oftentimes be seen much in advance of any destruction of the nerve-elements, has been adduced as strong evidence that the whole morbid process is primarily interstitial; whereas, in reality, the process may be primarily parenchymatous, giving rise to proliferation of the interstitial tissue secondarily, whilst the hyperplasia thus started may in its turn lead to destruction of other nerve-elements. According to this view, some of the nerve-elements suffer primarily, whilst others suffer secondarily to an interstitial-tissue proliferation originated by the primary degenerative changes in the one set of nerve-elements.

The view that the morbid process is primarily parenchymatous accords well with the growing belief that the disease is toxic in origin; for the effects of toxins on the nervous system are as a rule first manifested on some part of the neuron itself, whose destruction leads to secondary proliferative changes in the interstitial tissues. Dr. Mott suggests that it may well be that a lipolytic ferment attacks the myelin covering the nerve-fibres (*vide* p. 265).

Another view held by some is that the process is primarily vascular, and that the vessel changes lead secondarily to the other morbid conditions. This interpretation of the morbid picture was that adopted by Kindfleisch as long ago as 1863; and it has since found favour with different observers, including Ribbert, Buss, Williamson, Fürstner, Goldscheider, P. Marie, Hess, Bartsch, Phillipp Jones, and F. Schob, but is rejected by Tredgold. An argument which has been advanced in support of this hypothesis—namely, that a vessel with altered walls, and it may be even obliterated lumen, may be seen in the centre of the sclerotic patches—does not hold good in many cases, for patches may often be seen which are in no way related to vessels. Further than this, although vascular changes are met with in a considerable proportion of cases of disseminated sclerosis, in some recorded cases, otherwise typical, the vessels have not shewn any morbid change. Moreover, when vascular changes are present the most pronounced alterations may be seen in parts of the central nervous system quite free from any other morbid change, whilst well-marked degenerated areas may be in no way related to vessels. There is much then to suggest that the vessels may be affected by, say,



some toxin to which the other morbid changes met with in the disease are due; but that the vascular change can in no sense be regarded as the starting-point of all the anatomical changes, though some of them it may be.

A further hypothesis to be considered is that of Strümpell, who, as a result of two observations in which he met with a combination of hydromyelia, central gliosis, and multiple sclerosis, suggests that possibly disseminated sclerosis is not a disease of exogenous origin at all, but one truly endogenous; and again, that it is a multiple gliosis depending on congenital influences, such as are operative in the case of multiple neuroma, fibroma, lipoma, and the like. In support of his view he points out that nearly all nervous diseases of exogenous origin are characterised by early affection of the nerve-cells and axis-cylinders, multiple sclerosis being the only exception. He further contends that if the disease begins in the glia, without primary affection of the neurons, it is easier to understand why the myelin sheath suffers alone, and why the axis-cylinder may be so long preserved. Then again, the fact that the disease usually reveals itself in young persons, and that its first manifestations may be traced even to childhood, is regarded as significant in this connexion. Strümpell also points out that a disease may be thus endogenous, and yet the impetus to the disturbance may be the result of some exogenous influence; such as an acute disease or a trauma.

A careful review of the subject makes it clear that although in the present state of our knowledge the origin of the disease cannot be definitely decided, the weight of evidence is in favour of a parenchymatous degeneration of the nerve-elements as the primary process, with glial proliferation as secondary and reparatory. The occasional changes in the vessels can only be regarded, at most, as contingent elements in the disease.

**Symptoms.**—Three types of the disease are commonly described, a cerebrospinal, cerebral, and spinal, according as the morbid process affects both or one or other of these parts. In the majority of instances, however, so far as the central nervous system is concerned, the disease is general; and, though the earlier manifestations may be of cerebral or spinal origin, unmistakable evidence of affection of both of these parts appears sooner or later. It is exceedingly rare for the disease to be limited to the brain; and even older writers, such as Ross, admitted that, though psychical disturbances predominate in the cerebral form, the course of the disease does not otherwise differ materially from the cerebrospinal variety. In some cases the disease, throughout its clinical course, manifests itself by spinal symptoms only—there being an absence of cerebral symptoms, such as psychical disturbances, apoplectiform attacks, vertigo, nystagmus, and intention-tremor; but it is now fully recognised that sclerotic patches may be met with on necropsy scattered throughout the whole extent of the cerebrospinal axis, and yet their distribution may have been such as to give rise to the clinical phenomena of a spinal disease only. Exceptionally, the patches of sclerosis have been found

limited to the spinal cord, but it is always possible that in such cases they have been ill-defined in the brain, and have thus escaped detection. It appears best then to regard disseminated sclerosis as a disease which affects the whole central nervous axis, in unequal degree, it may be, in different parts, or earlier in some parts than in others; not as an affection in which any hard and fast line can be drawn between a form limited to the brain and one limited to the spinal cord.

The degree in which nerve-roots and peripheral nerves, both cranial and spinal, are involved varies greatly in different cases; but there is unquestionable evidence of their implication irrespective of affection of their nuclei of origin.

Far more important than any division of the disease into these three types is the recognition that its clinical manifestations may differ widely from those commonly regarded as characteristic; in aberrant cases few if any of the classical symptoms by which the disease first came to be recognised may be present. Dr. T. Buzzard has insisted on the extreme importance of recognising that such irregular instances of the affection occur; albeit most modern observers are agreed that from the cases formerly regarded as aberrant, another type of the disease may be constructed to which cases may be referred as commonly and as definitely as the former kinds of cases may be referred to the classical types. The importance of this observation is accentuated by the fact that many of the manifestations of the new type, to which attention is now being called, are often only to be distinguished from hysteria with great difficulty.

These aberrant cases did not escape the observation of Chareot and others of the older writers on this subject; for, since the discovery of the anatomical lesions of disseminated sclerosis, by Pitres in 1877, in two cases otherwise diagnosed during life, such anomalous cases ("*formes frustes*") have been recognised; yet it is only within recent years that the frequency of their occurrence has been appreciated. Women are more frequently affected than men, though cases of the kind occur in the latter sex also. It commonly happens that the first manifestations occur after some mental or physical shock. These may be but little observed at first; a peculiarity in the behaviour of the patient is readily ascribed to hysteria: for instance, there may be temporary aphonia; or sight might be impaired or lost for a time, and then recovered—a not uncommon mode of onset in these cases. Or it may be that a patch of numbness is noticed somewhere, perhaps so slight and so fleeting that it is only recalled to the patient's memory on close inquiry into the earliest manifestations of the disease. More rarely, subjective sensations of "deadness," "coldness," or "pins and needles" are first complained of. But perhaps the most common phenomenon noted in the early stages is loss of power in one or more limbs, usually evanescent, double vision is complained of, or some loss of control over the sphincter of the bladder is experienced, whilst less frequently the earliest manifestations consist rather in over-action, and thus convulsions may occur. However this may be, the all-important

point to be borne in mind in this type of the disease is that such initial symptoms may entirely pass off, to return with like abruptness at some subsequent period; or again, without entirely clearing up, they may diminish and remain in abeyance, it may be for years. It is no uncommon experience to hear that a patient presenting one or other of the above symptoms has quite recovered; but a few questions will usually elicit evidence that the disease, supposed to be cured, is only temporarily dormant. You hear that the patient, as a rule, walks quite well; but that when she gets tired she limps a little; or there is occasional double vision; or sight is not quite good at times, or the patient is sometimes rather hysterical in manner. Such symptoms are of grave import; and, to the experienced, indicate with certainty that there is but a temporary lull, and that at some future time, near or remote, the disease will once more assert itself with fresh vigour.

The physician who takes a grave view of such cases at the onset is for a time, for years it may be, regarded as having made a mistake in diagnosis; whereas those who regard the case as purely "functional" or "hysterical" are lauded for their acumen. After an absence, perhaps even for years, symptoms return, without obvious cause, during pregnancy or after parturition; under some debilitating influence, as of an acute illness of some kind; on some injury, exposure to cold, privation, or mental or physical shock. The original symptoms may return with greater intensity, or new symptoms may manifest themselves. Paralytic weakness may return in a limb previously thus affected; or may disable some other limb, alone or in conjunction with that first attacked. Again the symptoms may clear up, partially or almost entirely, to return once more at some subsequent period; or they may remain and continue to progress. But even when the symptoms thus persist, and even progress, this remarkable periodicity of the disease still manifests itself from time to time; transient improvements recur for a while, and false hopes are awakened.

Once fully established, the disease progresses with unerring certainty to death; though this may be long postponed, and there may be many periods of remission before the end is reached. Yet even at this advanced stage of the disease many of the classical symptoms of disseminated sclerosis may be wanting; and, in their absence, the inexperienced, while no longer doubting the organic nature of the disease, find it difficult to reconcile the picture before them with that of classical disseminated sclerosis.

On the other hand, such a patient may be quite bedridden with complete paraplegia, with or without spasticity and contracture; and the upper limbs, and even the neck muscles, may share in the loss of power. Groups of the affected muscles may waste. In areas of numbness there may be blunting of sensibility. Any movement may induce a sensation of giddiness. Sight may be extremely impaired, with or without evidence of a form of optic nerve atrophy to be subsequently described as characteristic of this disease. The tendon-reflexes may be exagger-



ated, and there may be ankle-clonus; more rarely the knee-jerks are abolished. The power over the sphincters may be impaired or completely lost. Such a patient may remain perfectly clear in intellect, but at times emotional; or, on the other hand, he may pass into dementia and fatuity. As advanced a stage of the disease as this may be reached, and even death may supervene, without nystagmus, intention-tremor, or a scanning utterance—features so prominent in the classical disease.

So varied are the clinical manifestations of disseminated sclerosis that indeed many types of the disease might be constructed in addition to the three which up to this point have engaged our attention. A brief allusion will be made to one or two of these after we have considered the classical types.

The disease, as portrayed by Charcot and most subsequent authors, has been conceived as follows:—The patient slowly falls into a spastic paraplegia with exaggerated knee-jerks, and, it may be, ankle-clonus. No real motor weakness of the arms occurs, but on any attempts at movement a curious intention-tremor of an irregular, jerky character is evoked. Closely allied to this is the nystagmus, which is either spontaneous in character or evoked only on lateral, on upward, or more rarely downward displacement of the globes. Diplopia, with paresis of some external ocular muscle, is among the paretic symptoms recognised as of no infrequent occurrence. An integral part of this group of symptoms is a peculiar defect of speech, described as a scanning utterance, in which the pauses between words, and it may be syllables, are increased with undue accentuation of the latter, and a tendency to elide the ends of words. The sphincter of the bladder becomes weak, and that of the rectum may be similarly affected. Apart from the occurrence of paraesthesias, in the form of numbness, coldness, pins and needles, and the like, sensory defects are rare. Amaurotic defects of vision may occur; there may be tinnitus aurium, and vertigo is common. Psychological disturbances occur in which the mental faculties become blunted; or there may be a manner suggesting a state of well-being quite out of keeping with the patient's physical condition. In a small percentage of the cases apoplecticiform or epileptiform seizures are met with. Trophic disturbances, muscular or cutaneous, are among the possible late manifestations of the disease; and, in the event of control being lost over the sphincter of the bladder, cystitis and pyelitis may result as final complications.

Instead of this slow mode of development the disease may begin most acutely, and all of the classical signs may appear with great rapidity, so that the patient is totally incapacitated by an amount of weakness and inco-ordination that makes walking, and even standing, impossible, and which renders the upper limbs equally useless, whilst marked impairment of vision, nystagmus, and paralysis of several cranial nerves may complete a remarkable clinical picture. A patient affected in this way may make what appears to be a complete recovery, but slight relapses occur from time to time over a period of many years, now

one symptom and then another, reminding us that the disease is only dormant, not cured. Or secondly, the clinical manifestations throughout may be those of a spinal cord affection; the psychical disturbances, vertigo, apoplectiform attacks, optic nerve atrophy, nystagmus, scanning speech, intention-tremor, and so on, being absent. There is always some form of motor disturbance in the legs, the amount of impairment of power varying in different cases. The defect is usually of the spastic type, with exaggerated knee-jerks, and perhaps ankle-clonus; but sometimes there is an absence of spasticity, and not only may the knee-jerks not be increased, but they may be actually abolished; in the latter case they may disappear and reappear at intervals. There may be unsteadiness, titubation as in cerebellar disease, or actual ataxia. Various paraesthesias may be complained of; and sometimes these are accompanied by actual blunting or loss of sensibility, of variable distribution. There may be some difficulty in passing water early in the course of such cases, or there may be some loss of control over one or both sphincters. If the morbid process invade and destroy the anterior-horn cells of the lumbar enlargement, groups of muscles may become atrophied. Trophic disturbances of the skin, in the form of bed-sores, belong to the later stage, and are associated with loss of control over the sphincters. From the above description it will be manifest that this type of the disease is easily confounded with motor neuron disease, combined degeneration, and tabes dorsalis. The points on which we have to rely for diagnosis will be discussed subsequently. Once more, instead of the more usual chronic progress of the malady, the paraplegia and its attendant symptoms may develop so acutely as to simulate a transverse myelitis, or such a state of things may result at any time during the otherwise chronic course of a case. Then again hemiplegia may be the predominant symptom, though this variety is not common, and the hemiplegia is as a rule transitory.

The rarest form of the affection is that which simulates the motor neuron disease formerly known as amyotrophic lateral sclerosis in its clinical manifestations. Cases of the kind have been recorded by Pitres, Dejerine, Skolossnow, and Probst.

It can serve no useful purpose to multiply clinical types of this disease unnecessarily; but one other deserves brief notice owing to the frequency of the cases. Here the symptoms all point to a spinal cord affection, with the exception of the peculiar form of optic atrophy, which probably affects chiefly or solely the temporal halves of the discs. Some such cases—in which the knee-jerks are absent, and shooting pains, ataxia, and Romberg's sign are present without psychical disturbance, scanning speech, nystagmus, or intention-tremor—may be mistaken for cases of tabes; but there is usually sufficient evidence of loss of motor power without muscular atrophy to prevent this error.

Finally, we must remember that cases often fall away from the spinal type; that, as Charcot insisted as long ago as 1876, paraplegia may be an almost isolated symptom, to which, however, may be added some of the other signs of the disease; and that it is exceptional not to find

two or three of the characteristic associated phenomena in some stage of the disease.

It is scarcely necessary, or even desirable, to construct a type for the third or mixed form of the disease; for, as I have said, the disease is cerebrospinal in its distribution, and sooner or later will present symptoms of a mixed character accordingly.

So manifold are the phenomena of disseminated sclerosis that it behoves us to consider in detail the various symptoms that may arise.

*Motor Disorders.*—Fatigue.—Claude and Egger have insisted on rapid fatigue on sustained muscular effort as an important initial symptom, and it must be a common experience that what appears to be neurasthenia proves, on examination, to be disseminated sclerosis. They found that the upper as well as the lower extremities behaved in this way.

Tremor.—One of the most characteristic features of the ordinary form of the disease is a peculiar irregular jerky tremor which only occurs on attempts at movement, and ceases as soon as the muscles are at rest again. It was present in 75 per cent of the cases collected by Probst. At the beginning of the act the tremor is as a rule slight; but it increases in range until, when the object aimed at is all but or actually attained, it reaches its height; at this stage the to-and-fro jerkings may be of the wildest possible character. The excursions are large and are slowly rhythmical. The tremor is not limited to the muscles actually in action, but spreads to neighbouring ones; so that if the arm is being moved there may be not only tremor of it, but also of the head and upper part of the trunk. Whilst, as has already been said, these cases may be under observation for years without any tremor being detected, no part is exempt from it on attempts at movement. It may be seen in the facial muscles, in the ocular muscles as nystagmus, and laryngoscopic examination may reveal similar tremor of the vocal cords on phonation—a condition of things which is also evidenced by a tremulousness of the voice. The tremor of the neck muscles causes oscillation of the head; and, as this goes on while the head appears to be at rest when the patient is sitting, this seems to form an exception to the rule that the tremor only occurs on movement; in reality the neck muscles are not at rest, for though the patient is sitting still, the neck muscles are constantly in a state of action as they support the head in the erect position. In such cases immediately the patient lies down the tremor ceases, to return, of course, on any attempt to sit up. In no part of the body is the tremor more commonly present than in the arms, so that if the patient attempts to touch the point of the nose with the tip of the index finger of the extended limb unsteadiness may only be observed towards the completion of the act, whereas in severe cases it begins with the voluntary movement, and becomes of wide range by the time the tip of the nose is reached. The handwriting is altered in a characteristic manner; for the first words of a sentence may be readable, whilst, owing to the increasing unsteadiness of the hand, the sentence becomes more and more illegible as it proceeds. The trunk may oscillate when the patient sits or stands, and



the respiratory muscles may be affected, resulting in jerky breathing. When present in the legs the tremor is evoked by standing, or when the patient begins to walk; but it may also be brought out if, when the patient is in the recumbent posture, he be made to raise the leg off the bed to attempt to touch some object held above it.

The intention-tremor may give rise to ataxic movements indistinguishable in themselves from those of true ataxia due to sensory defect; and the similarity is increased by the fact that in some cases the patient can stand if supported, but falls if left to himself. Both conditions are, however, readily distinguished from true ataxia as closure of the eyes does not in any way affect them. Strümpell, however, regards the intention-tremor as an ataxic disturbance; and in a boy with tumour of the corpora quadrigemina, observed by Bruns, there was intention-tremor of the arms and ataxia of the legs. So too Goldscheider has observed cases in which disseminated patches of sclerosis, especially in the pons, caused acute ataxia, which afterwards assumed such characters that it became impossible to distinguish it from intention-tremor. Claude and Egger consider that ataxia is more common than many of the recognised classical symptoms including intention-tremor. No satisfactory explanation of the mode of origin of the intention-tremor has yet been offered. Charcot's view was that the axis-cylinders, denuded of their myelin sheaths, offer different degrees of resistance to the passage of impulses at different points in their course; so that such impulses are variously retarded in different axis-cylinders, and, reaching the muscles in an irregular manner, thus evoke irregular contractions of them. This explanation is supported by two observations by Sir W. Gowers in which, probably as a result of pressure on the motor path, intention-tremor was present in a case of a tuberculous growth in the crus; and in another case of a similar growth in the pons.

Lib is of opinion that the tremor depends on the precise position of the patches of sclerosis, where it disturbs some mechanism for the co-ordination of movement. In support of this view it has been said that the symptom is absent when the sclerosis is limited to the spinal cord, but occurs when the pons is affected. Stephan, on the other hand, regards the optic thalamus as the seat of lesion in such cases; according to Oppenheim, a similar form of tremor is met with in cases of cerebellar tumour. This I have seen; and, moreover, after ablation of the cerebellum in animals the oscillation of the head on any attempts at movement strikingly resembles that seen in disseminated sclerosis. Of all the possible explanations that have been offered of the way in which the intention-tremor results, none appears to me so satisfactory as that which supposes it to be due to a failure of synergic action of muscles in purposive movements consequent on an unequal degree of innervation both of the muscles directly concerned and of their antagonists.

Apart from the irregular jerky movements on the performance of voluntary acts, spontaneous movements sometimes occur over which the patient has no control, as in a case recorded by Bouchaud. Attacks of

hiccup, yawning, laughing, or crying may occur; and the latter phenomena are as a rule unattended by the corresponding emotional feelings. Such conditions may be met with early in the course of the affection, and a slight degree of this state of things is not uncommon. In that lesions of the medulla and pons are so commonly associated with emotional phenomena, it is probable that the occurrence of such emotions in disseminated sclerosis is consequent on patches of sclerosis in these parts of the central nervous axis.

*Rigidity.*—Spasm of the muscles is one of the most frequent symptoms of the classical type of multiple sclerosis. Though the arms do not escape, the legs are more commonly affected, and in greater degree. Spasm in the extensors preponderates at first; but the flexors ultimately gain the ascendancy and lead to permanent contracture, in which the legs may be so drawn up that the heels are pressed against the nates. Contracture of this kind in the arms is rarely seen. Even before contracture voluntary movements are hampered by the rigidity; and the latter increases with movement, so that it may ultimately prevent the possibility of further movements for a time. Passive movements produce the same result.

*Tendon-jerks.*—With this condition of rigidity the tendon-jerks are in excess of the normal; but it may so happen that the full effect of this increased irritability is masked, or altogether obscured, by the spasm actually preventing the responsive movement in the limb which would otherwise result from a tap on the tendon. The increased activity of the tendon-jerks may be manifested by an excessive jaw-jerk, amounting even to clonus; and by excessive arm-jerks and knee-jerks, with, it may be, rectus-clonus and ankle-clonus. On the other hand, in a small number of cases the knee-jerks are abolished.

*Motor Paralysis.*—Some motor weakness is common to all the clinical types of disseminated sclerosis; but no symptom is more variable as regards its mode of onset, the degree of impairment, and its precise behaviour. These variations have been sufficiently insisted on when discussing the type of the disease so apt, more especially in its earlier stages, to be mistaken for the manifestations of hysteria. The motor weakness may or may not be associated with tremor or rigidity, but in either case the weakness rarely amounts to considerable paralysis. As a rule all movements can be executed, though feebly, slowly, and with difficulty; and, as fatigue is soon induced, the first movements attempted are always performed better than subsequent ones. Though no part is exempt from loss of motor power, the legs are most commonly affected; the arms, however, suffer almost as frequently, but, as a rule, later. The weakness is most commonly associated with rigidity in the legs, and with jerky tremor in the arms. The latter association also occurs in the neck muscles, when they are affected, and with the muscles of the eyes, and it is probable that the peculiar defect of speech depends on the same association. Paresis or paralysis may also occur in other regions, more especially in the territories dominated by other of the cranial nerves. Besides ocular paralysis, the motor division of the fifth cranial nerve may

be affected, resulting in difficulty of mastication ; thus, the facial muscles may be palsied as a result of a lesion interrupting the motor path at some point on the cerebral side of the facial nucleus, or involving the nucleus or emergent fibres of the nerve.

Sclerotic patches in the medulla may lead to difficulty of swallowing, associated with paralysis of the palate which may be unilateral or bilateral ; and, alone or in conjunction with such defects, paralysis of the vocal cords may exist, when the abductors suffer alone or before the adductors ; but Réthi refers to 15 cases out of 44 in which there was adductor paralysis, in many of which the tensors of the cords were also affected. The tongue may shew the paralytic deviation due to a lesion interrupting the motor path to it at some point on the cerebral side of the hypoglossal nucleus ; or the lesion may be in the medulla affecting the nucleus or emergent fibres of the hypoglossal nerve, when atrophy on one or both sides of the tongue results, according as the lesion is unilateral or bilateral. In consequence of defects of the same kind in areas of sclerosis in the medulla various articulatory defects of speech are met with ; alterations of tone of voice also, and, it may be, suffocative and other attacks which endanger life.

Curious apoplectiform attacks sometimes occur, and may give rise to hemiplegic weakness, indistinguishable from the result of rupture or occlusion of a cerebral artery, save by its fleeting character ; in this it closely resembles the apoplectiform seizures in general paralysis of the insane. A further resemblance to the attacks in general paralysis is seen in the tendency to repetition of these attacks. The hemiplegia, as a rule, is of the ordinary form, and may be accompanied by aphasia ; or there may be alternate paralysis, the limbs being affected on one side and the territory presided over by some cranial nerve on the other.

*Gait.*—Paralysis, whether spastic or flaccid, may be in such degree as not only to forbid walking, but to exclude all possibility of standing ; but when progression is still possible the most varied gaits are met with. The most common of these is a spastic paralytic gait in which the combination of weakness and rigidity hamper the movements. The inferior extremities are slightly flexed, and cling to each other and to the ground, so that they are unlocked with difficulty ; and, as they are brought forward in turn, the anterior half of the foot scrapes along the floor. On the other hand, there may be a combination of spasticity and unsteadiness ; so that, in addition to the clinging of the feet to the floor and the difficulty of moving the lower extremities, the patient stands on a wide base, and, as every movement is uncertain and reeling in character, he tends to fall. Closely similar to this state of things is the combination of spasticity, paresis, and ataxia, described by Oppenheim, in which the legs are stiff and held widely apart from each other ; the movements are slow and the anterior half of the foot clings to the floor, but once it has been effectually released the limb is sharply raised in the air and the heel is stamped down. The same observer has noticed an ataxic condition in one leg and a combination of spasticity and paralysis in the other. Much



more rarely a purely cerebellar gait is seen, in which there is mustadiness, titubation, and reeling like a drunken person. Or the gait may be more or less ataxie in character. Apart from hemiplegic weakness of apoplectic origin, one leg may be affected alone; or one may be more affected than the other: thus all sorts of curious combinations are seen, giving rise to the most grotesque modes of progression. Rapid variations in the character of the gait and in the degree of defect occur in consequence of the sudden changes and variations so characteristic in all the symptoms of multiple sclerosis; and in many cases all that is observed in the earlier stages is a feeble gait having no peculiar characteristics other than those common to all conditions attended with feebleness of the lower extremities without spasticity.

*Speech-defects.*—"Scanning," "staccato," or "syllabic" speech is one of the symptoms of the classical disease, and was supposed to be frequent. In reality, however, many cases do not present any alteration in speech; and the majority of patients who do, only speak slowly without the scanning character being distinctly marked. When typically present it is very characteristic; the words are uttered slowly, the syllables, and more rarely the words, have the pauses between them lengthened, and each syllable is unduly accentuated, though there is a tendency to elide or slur over the ends of words. The speech may have a nasal character in consequence of paresis of the palate; but, apart from this, the pronunciation of certain letters is also somewhat indistinct, especially the voiced explosives such as *b*, *d*, *g*, and the extra fricatives *c* and *r*, which are to be produced by the second and third stop-positions described by Prof. Wyllie. The voice is monotonous, according to v. Leube, in consequence of the inability to alter quickly the height of tone and accentuation of syllables. Moreover, according to the same observer, such patients are unable to maintain any tone in its full intensity for any length of time; the note gets higher and higher, possibly from failure to regulate the tension of the vocal cords in response to the increasing strength of the expiratory blast. Occasionally there is aphonia; or speech may be interrupted from time to time by noisy inspiratory sounds consequent on incomplete opening of the glottis, but true aphasic defects are very rare.

As in respect of other muscular movements, the first words of a sentence are often much more clearly spoken than those at the end, when the muscles of speech become fatigued. Indeed this abnormal tendency of the muscles to tire is one of the factors in the causation of the syllabic utterance. Not only may the muscles of the lips, tongue, palate, and larynx be at fault, but also those concerned with the respiratory movements. The researches of Goldscheider are of great interest in this connexion, for he has shewn, by the graphic method, that the curve produced by the expiratory blast is flat and not steep as in the normal, and that the line of the curve is wavy, a condition ascribed to oscillations of the vocal cords, whilst a similar inability to control the tongue was demonstrated by making the patient vocalise "r"; for instead of small regular oscillations none were present in the first part of the

curve and they were imperfectly marked in the latter part of it. A similar difficulty was demonstrated with explosives, in which case the steepness of the rising curve depended on the time the patient had to prepare before uttering the sound.

*Mental Symptoms.*—Emotional disturbance, defective memory, and slowness of thought are common, and, according to some writers, a large percentage of cases present even more serious mental symptoms. Racecke, Seiffer, Lannois, and others have recorded such cases. According to Racecke, when mental symptoms occur early, depression and maniacal disorders, with delirious episodes, confusion, hallucinations, and isolated delusions, are most common; whilst when they occur at a more advanced stage of the disease, expansive delusions, with the exaggerations and lack of judgment of the general paralytic, are more usual. Some caution is, however, needed in this connexion, for Hunt and others have recorded cases in which disseminated sclerosis and general paralysis of the insane have both affected the same patient.

*Ocular Phenomena.*—So important are the ocular phenomena of disseminated sclerosis, more especially in their bearing on the difficult problem of diagnosis, that they call for our most careful consideration. Disturbances of vision commonly occur, and may or may not be accompanied by changes in the optic nerves, perceptible on ophthalmoscopic examination. Such patients usually complain of a mist before their eyes, rarely of specks and flashes. The defect in vision may be of very rapid onset, in some cases, indeed, quite sudden; and it may be the earliest manifestation of this mysterious disease; on the other hand, it may be of slow and gradual onset. Whatever the rate of progress, the same variability is met with in this symptom also; the most marked amblyopic disturbance may be followed by a period of remission in which vision is greatly improved, and then later the defect becomes as bad as ever again. Many such relapses and improvements may occur in the course of the disease before permanent amblyopia is established. It is common to meet with cases in which transitory defect of vision, never amounting to complete amblyopia, has existed in one eye, for, it may be, some months or a few weeks only, which has then cleared up, but is followed at some subsequent period by precisely the same defect in the opposite eye; or indeed in the eye originally affected.

Of the anomalies of the fields of vision central scotoma for colours is a prominent feature. Uhthoff found central scotoma in 15 out of 24 cases of this disease. Another alteration of the fields which occurs is that of peripheral limitation; and Uhthoff found this contraction of the fields in 11 out of 24 cases.

Both the transitory amblyopia and the contraction of the visual fields are symptoms which may readily be mistaken for indications of hysteria in a disease in which, as we have already seen, there are many manifestations indistinguishable from those of the functional disorder; it therefore becomes all-important that in any case in which these phenomena are met with, a careful search should be made by ophthalmoscopic

examination for changes in the optic nerves. The most common change in them is pallor, often so slight in the earlier stages as to be difficult of interpretation; at this time any inequality in the degree of affection of the two nerves may be of the most important pathological significance. Though the occurrence of optic atrophy did not escape the observation of Charcot, and of others who have studied disseminated sclerosis, no one has made so exhaustive a study of this phase of the affection as Uhthoff. Among previous observers, however, Guanck's statistics, quoted by Ross, must be mentioned; for of 50 cases which he observed there were defects of vision in 28, and changes in the optic discs in 15; these defects were atrophic in character in all but 3, in which there were hyperaemia and neuritis. Uhthoff found changes in the optic nerves in 45 per cent of 100 cases of disseminated sclerosis which he examined ophthalmoscopically. In 2 of the cases there was marked atrophy of both nerves; in 1 a similar atrophy existed on one side with pallor of the temporal side of the opposite disc. In 7 cases the whole of the disc was incompletely atrophic on both sides; in 4 this change was seen in one eye only, while the temporal side of the other disc was pale; in 8 cases the change could be detected in one eye only. In 18 cases the atrophy was partial, and was limited to the temporal half of the disc; and in 5 there was distinct evidence of optic neuritis—well marked in 3, and slight in 2. Dr. T. Buzzard's figures closely agree with those of Uhthoff; out of 100 cases of disseminated sclerosis there was pallor of the discs in 43 per cent. The same observer has never met with anything that might strictly be characterised as optic neuritis or papillitis; though he has seen what he has described as a dark-grey discoloration "somewhat resembling the tint of hyperaemic grey matter of the cerebrum." Whilst this intense hyperaemia probably represents a stage in the process which subsequently results in atrophy, it is probably never present in the large majority of cases. When such a change is seen with the ophthalmoscope, it depends no doubt on affection of the optic nerve, at its termination in the globe, by a patch of sclerosis resembling that which occurs in other parts of the nervous system. On the other hand, when, as is the rule, there is pallor of that portion of the nerve which forms the disc, there is strong evidence that this atrophic condition of this portion of the nerve depends on a patch of sclerosis situated at some portion of the nerve behind the globe, or affecting some portion of the optic commissure or tracts. Sir W. Gowers dissents from this, and regards the atrophy in these cases as strictly comparable with that met with in tabes and as due to a primary degeneration of the nerve-elements. The weight of evidence is, however, strongly opposed to his view. I have never seen optic neuritis in disseminated sclerosis, and in attempting to estimate the incidence of the condition much difficulty has been experienced, because writers on the subject have not always made it sufficiently clear whether the term optic neuritis is used to denote a papillitis, or whether retro-bulbar neuritis is also included in their figures. The distinction is important, for the phenomena ascribed to retro-bulbar



neuritis are common, whilst papillitis must be rare. The most notable contributions to the subject have been by Uhthoff, Fleischer, Bruns and Stolting, Kampherstein, Bagh, Schley, Oppenheim, and Frank, all of whom have met with instances of optic neuritis in this disease.

Two classes of cases still remain for our consideration. In one of these, amblyopic defects of vision are complained of by the patient, attended, it may be, by alterations in the fields of vision on perimetric observation, but in which ophthalmoscopic examination fails to detect any abnormality in the optic discs or other parts of the fundus. Such cases may lead to grave errors of diagnosis, as the failure on ophthalmoscopic examination to detect any objective cause for the amblyopia may lead us to regard the case as one of hysteria; whereas the amblyopia may depend on a patch of sclerosis situated in some part of the nerve or tracts behind the globe,—a condition that has not existed long enough to lead to secondary atrophy of the termination of the part of the nerve which forms the optic disc. The other class of cases consists of those in which, though distinct pallor of the disc is obvious on ophthalmoscopic examination, there is normal acuity of vision. Though subsequently amblyopic defects of vision may be met with in such cases, it is wonderful for how many years the detection of such a pallor may precede defective vision. Indeed, in the absence of all other signs of disseminated sclerosis the true significance of the pallor of the optic discs may not be appreciated.

All these disturbances of vision have been traced to changes in the optic nerves and tracts; no sclerotic or other changes in the retina have ever been described in this disease.

Besides the defects of vision, affections of the ocular muscles occur; they consist either in nystagmus (see art. "Medical Ophthalmology," p. 334), or in paralysis of one or more of these muscles. In the type of the disease portrayed by Charcot and earlier writers nystagmus is one of the leading features; but we now know that in a very large number of otherwise typical instances of disseminated sclerosis nystagmus forms no part of the clinical picture. Nevertheless, it occurs in about half the number of cases of the disease, according to Charcot, and in 70 to 80 per cent according to Marie; whilst Uhthoff found it in 58 per cent of his cases, and Krafft-Ebing in 60 per cent of his. The nystagmus is usually bilateral, but in rare cases it may be present in one eye only. Most commonly it occurs only when the eyes are moved; but it is present sometimes apart from any attempts at voluntary movement of the eyes, and consists, as a rule, in short horizontal jerks to which some vertical or rotatory tendency may be added. It becomes intensified on turning of the eyes to either side, though this increase may be more marked when the eyes are turned in one direction than in the other, and when more marked in one eye than in the other it is so in that which is turned outwards. Similarly, attempts at fixation as an object is brought nearer to the patient intensify it; and, like other voluntary movements of the eyes, they may evoke nystagmus when in the resting condition of the

globes it is not present ; or an upward or downward movement of the eyes may bring the symptom about, in the latter case, however, but rarely ; such phenomena we are in the habit of calling "nystagmoid" jerks or movements, as opposed to the spontaneous nystagmus which requires no such devices to call it forth. Nystagmus may only occur on turning the eyes laterally to one side ; or, although it may occur when turned in either direction, the movement to one side may evoke a greater degree of unsteadiness than movement in the opposite direction. We must not mistake for the nystagmus of multiple sclerosis the slight nystagmoid jerks common in debilitated states such as convalescence from some severe illness. Nor should we mistake the slight jerky tremulousness of the globes, seen on lateral deviation in hysterical cases, for the nystagmus of organic disease. The functional form of the condition is commonly associated with a blinking movement of the lids ; this combination is very characteristic, and should prevent all chance of error.

Ocular paralysis may be actually present when the patient comes under observation ; or it may form part of the previous history, and have been recovered from, thus resembling the state of things met with in tabes. Unthoff found marked paralysis of the ocular muscles in 17 per cent of his cases ; and in half of these the character of the paralysis pointed to its nuclear origin. Isolated paralysis of the sixth nerve was more commonly met with than a similar affection of the third. The power of conjugate movement of the eyes to one side, or of convergence, is most frequently impaired or sometimes lost. When single nerves are involved the sixth is most commonly affected on one or both sides ; less frequently there is progressive paralysis of the third, or occasionally the fourth may give evidence of defect.

The pupils are often equal ; but one may be larger than the other, or such inequality may only appear on accommodation. Failure of the pupil to react on accommodation is more common than loss of its reaction to light ; but both conditions are exceptional.

*Sensory Symptoms.*—Although sensory defects are not so prominent as the motor, in reality they are rarely absent in some form or other. The most common is giddiness, which may be one of the earliest symptoms, and in which it appears to the patient that he and the surrounding objects are both going round. It may persist for long periods, or may only occur more or less in paroxysms. Patients so affected often find that they remain free from giddiness as long as they can keep still ; but that any movement, even such as putting out the arm to reach a book at the side of the bed, will bring on an attack, which, however, passes off after they have remained quiescent for a little while.

Headache usually occurs in paroxysms ; and the pain, though as a rule moderate, may be severe, and may be referred to the back of the head and down the neck, or to the vertex, or the forehead. Such pain is sometimes associated with vomiting, and in some cases there may be unilateral headache, as in hemiplegia.

Of cutaneous sensory disturbances paraesthesias are the most common,

and may affect any part of the body, including the areas of supply of sensory cranial nerves; though the hands and feet are most commonly affected. The mucous membranes may participate in these defects. Probably no subjective feeling is more common than that of numbness, which, though sometimes associated with objective blunting of sensibility, commonly exists without the possibility of detection. Feelings of pins and needles, or as if the part had gone to sleep, are common; and various feelings of heat and cold occur. Though such sensations give rise to discomfort, this is in no way comparable to the distress which is sometimes occasioned by cramp-like feelings, which are likened by some patients to a slow twisting and pulling asunder of the parts of the limb on a rack. The concomitance of the most marked feelings of numbness in the same limb with these exerting paroxysms of cramp-like pains gives rise to mixed feelings of the most distressing character. Sometimes pain in the spinal column is complained of, and in a patient under my observation with severe pain in the groin walking always evoked it, but it disappeared after a short rest; the pain, however, came on spontaneously from time to time quite apart from movement of the limb. Girdle feeling is rare, so are the lancinating pains and gastric crises of tabes.

Objective defects of sensibility are said to be rare, and with the most pronounced subjective sensations, even of numbness, no blunting of sensibility may be detected. It is probable, however, that such objective defects of sensibility are often missed as they are so fleeting; so that, although not present on one examination, repeated systematic examinations may prove their existence from time to time in the course of the disease. It is not uncommon to find most marked anaesthesia and analgesia in some part one day, and to find no trace of it on another; and so on. I have met with slight blunting to painful impressions where tactile sensibility appeared to be quite normal. All forms of sensibility may be affected, including an inability to distinguish heat from cold; and these abnormalities, like the paraesthesias, are most commonly found affecting the hands and feet. Permanent anaesthesia may occur. Hemianaesthesia is sometimes met with, and may be a hysterical manifestation added to the organic disease; but, on the other hand, permanent anaesthesia of the kind may depend on a patch of sclerosis in the fillet interrupting the sensory path to the brain on one side. Freund found sensibility affected in 21 out of 33 cases; in 14 of these the defect was transitory, in the others it was lasting.

Claude and Egger found considerable disturbance of osseous sensibility, and the duration of osseous perception was sometimes ten times less than normal. Muscular sense may be affected, apart from the existence of cutaneous anaesthesia or in conjunction with it; all notion of the whereabouts of a limb or the position of its component segments being lost. Disturbances of this kind were present in 22 of Freund's cases.

*Superficial Reflexes.*—Absence of the abdominal reflexes is an important



indication of the disease, as has been pointed out by Strümpell, who found them absent in 67 per cent of 24 cases of disseminated sclerosis; whilst out of 185 persons with normal nervous systems they were only absent in 13·5 per cent. In Probst's series these reflexes were not obtained in 73 per cent of the cases. Important as is this observation it cannot be said to compare with that which relates to the plantar reflex, for there is no more valuable sign of the disease, notably in its earliest stages, than the extensor type of reflex (Babinski's sign), so commonly present, for it serves to prevent the grave mistake of regarding this serious disease as hysteria.

*Trophic Disturbances.*—Though such defects are not frequent in multiple sclerosis, some degree of vasomotor disturbance is more common than is generally supposed. Of 10 cases of erythromelalgia recorded by Dr. James Collier, no fewer than five and possibly six of the patients had disseminated sclerosis. Comparatively early in the course of the disease there may be oedema of the feet and ankles, which may persist to a slight extent even when the limbs are in the horizontal position; or they may then disappear and only reappear after these parts have been dependent for a time. Swelling of joints may occur, especially the small joints of the hands and feet; and bleb-like blisters may occur in the skin. There may be abnormal local depression of surface temperature, as of a limb, and this may be attended with sweating. Trophic disturbances of so severe a character as to lead to the danger of bed-sores is only a part of the final stages of a protracted case in which there is usually loss of control over the sphincters; a condition which has played no unimportant part in bringing about this state of affairs. The nails may become brittle and crack; and the hair is said to fall out in some patients. Muscular atrophy is only met with in a small group of cases. Such atrophy may involve many muscles, but is more commonly limited to certain groups, especially the small muscles of the hand.

*Bladder and Rectal Troubles.*—Quite early in the course of multiple sclerosis there is commonly some difficulty in holding or passing water; and, according to Oppenheim, the majority of cases present some slight degree of rectal as well as vesical trouble. Any marked interference with these functions, however, usually occurs late in the course of the disease, when there may be complete loss of control over one or both sphincters. When these disorders occur early they present a markedly remittent character; and there may be incontinence or retention of urine without any affection of the anal sphincter, the former defect being by far the commoner.

*Sexual Disturbances.*—Increased excitability of the sexual functions may be met with; but some degree of weakness or loss of sexual power is more common, and may occur comparatively early in the disease.

*Other Organs.*—The other organs of the body do not present any evidence of disease associated with the condition of the nervous system; but with patches of sclerosis occurring in the medulla it is not surprising

that palpitation and dyspnoea should be noticed. Glycosuria sometimes occurs, and has also been found associated with patches of sclerosis in the medulla.

**Course and Duration.**—P. Marie has distinguished four modes of progression in this disease: (1) A chronic progressive course; (2) A chronic course with sudden intercurrent attacks of visual disturbance, apoplectiform seizures, hemiplegia, and the like; (3) A chronic remitting course; (4) Increasing improvement or apparent cure.

From the description of the manifestations of the disease, it is obvious that the third of these modes is the most common; and excluding the fourth group, which probably does not deserve consideration except as part of the third, the least common mode is that included under his second group.

We have seen how common it is to meet with periods of arrest, or even of improvement amounting in some cases perhaps to apparent cure. And we have also seen how such remissions are followed, after a variable time, by relapses; several such improvements and relapses possibly occurring in the course of the same case. That no hard and fast line can be drawn between such cases characteristic of Marie's third group and his fourth is obvious in that although he includes in the fourth group only the cases in which there is apparent cure, we have seen abundant evidence that, after long periods of arrest, exacerbations occur; and probably no case of true multiple sclerosis ever ends in recovery. The chronic progressive mode of Marie's first group is characteristic of the classical type of the disease, and is next in frequency of occurrence to the chronic remitting mode. Charcot has described three stages in the course of this chronic progressive mode: the first from the time of onset until the spastic paralysis and tremors are established; the second in which the patient is more or less confined to bed, the spastic paralysis has gone on to contracture, and all the symptoms of the first stage are further advanced;—this is a stage of the disease which may last for many years, during which the nervous symptoms do not progress materially, and the patient's nutrition is well maintained; the third stage is characterised by general nutritional disturbances, loss of appetite, emaciation, and tendency to bed-sores; the psychical disturbances are far advanced, the speech-defect is more marked, the sphincters are paralysed, cystitis sets in, bed-sores form in neglected cases, and death results from pyæmia.

Whatever the mode of the disease, this final stage is common to most cases of disseminated sclerosis. Some intercurrent affection, however, such as pneumonia, pleurisy, or pulmonary tuberculosis, may prove fatal; in some cases, again, death is caused by bulbar paralysis consequent on patches of sclerosis located in this part.

Nothing is more difficult than to fix the *duration* of the disease; the diversity is too great. All that can be said is that the duration is to be reckoned by years; and that, according to Charcot, whose statement has been confirmed by subsequent writers, patients in whom "spinal"

symptoms alone are present may live for twenty years or more after the first manifestations of the disease.

**Diagnosis.**—Easy as is the diagnosis when the clinical manifestations are those so graphically depicted in Charcot's classical account of the disease, it is nevertheless a matter of extreme difficulty in many aberrant cases of the affection, a group which, as we have already seen, is even larger than that of the so-called typical cases.

*Hysteria.*—Of all conditions of the nervous system none is more likely to be confounded with disseminated sclerosis than hysteria. Dr. T. Buzzard's statement—that disseminated sclerosis in its earlier stages is of all organic diseases that most commonly mistaken for hysteria—has every justification. The combination of symptoms unconnected with any one system and independent of anatomical distribution, in conjunction with the rapid variations and changes of the manifestations of the disease, makes it easy for the two conditions to be confused. Both are met with most commonly in early adult life, and both may appear to depend on some mental shock, either alone or combined with some physical injury, perhaps of the most trivial character. Scanning speech and intention-tremor may both be met with in hysteria; and it has been said that nystagmus also may occur in this affection. The latter statement is, however, probably erroneous; for in an extensive inquiry into the distinguishing features which characterise these two diseases, Souques never found this symptom present in hysteria. To a form of jerky unsteadiness of the globes, commonly associated with blinking of the lids which may occur in hysteria, I have already alluded. Our difficulties in diagnosis are intensified by the frequency with which hysterical manifestations supervene upon the organic basis; in such amount, it may be, as effectually to obscure the underlying structural defect and make errors in diagnosis of common occurrence.

On what points then are we to rely for a diagnosis between two conditions so easily confounded? Of great importance, if present, is the detection on ophthalmoscopic examination of changes in the optic nerves; or, failing this, of a certain character of defect of vision. In both diseases disturbances of vision occur, but in hysteria no structural changes exist in the optic nerves. Another important sign is the detection of distinct nystagmus, which probably never occurs in hysteria; and, when present in disseminated sclerosis, is of great diagnostic value. Loss of control over the sphincters usually occurs early, and thus aids our diagnosis; though they may not be affected until later in the course of the disease, after other symptoms characteristic of the organic affection have manifested themselves, and diagnosis is no longer in doubt. Another phenomenon which may occur early, and thus help us in diagnosing the organic affection, is the abolition of one or both knee-jerks,—a state of things which is, however, comparatively rare. Before all these indications must be placed the alteration of the plantar reflex to the extensor type (Babinski's sign) owing to its early and almost invariable occurrence in the disease.

The well-known stigmata of hysteria when present, though leaving



no room for doubt that there is this functional element in the case, unhappily do not aid us in determining whether the functional manifestations have an organic substratum. Similarly, the influence of suggestion in modifying or clearing up the symptoms does not materially alter the position of doubt in which we may find ourselves.

*Cerebellar Disease.*—The fact that patches of sclerosis may occur in the cerebellum or its peduncles and give rise to cerebellar symptoms in disseminated sclerosis makes it necessary for us to recognise what symptoms should guide us in our attempt to distinguish these cases from those in which the cerebellum or the cerebellar system is the sole seat of the morbid process responsible for the clinical picture. An outstanding feature in the cerebellar cases is the absence of spastic paralysis, and although the tendon-jerks may be unduly active, ankle-clonus is not to be expected. Moreover, the superficial abdominal reflexes are not abolished, and the plantar reflex should usually remain of the normal flexor as opposed to the extensor type that is so constant in disseminated sclerosis. Subjective and objective defects of sensibility form no part of the clinical picture, and the sphincters are not affected. Moreover, the remissions and relapses met with in disseminated sclerosis do not occur, although some forms of disease of the cerebellum permit of improvement. As in Friedreich's ataxia, a familial tendency may further serve to distinguish some forms of cerebellar disease from disseminated sclerosis.

*Hereditary Ataxia.*—As it is said that disseminated sclerosis may occur in quite young children, it is sometimes difficult to distinguish between this condition and Friedreich's ataxia. A few instances have been recorded in which more than one member of the same family has been the subject of disseminated sclerosis; but this affection cannot be said to be a family disease, so that the occurrence of symptoms in more than one member of the same family is a diagnostic point of importance. Of further value in diagnosis is the absence of knee-jerks and the detection of any bodily deformity such as lateral curvature and pes cavus.

*Pseudosclerosis.*—Cases have been described in which there was the clinical picture of disseminated sclerosis during life, but no changes were found after death to account for the condition. The exact nature of these cases is doubtful, and they are far too rare to be of much importance. For this subject the reader is referred to p. 847.

*Paralysis Agitans.*—So totally different are the pictures of the two diseases, that in spite of tremor being common to both, their distinction is not difficult. Paralysis agitans occurs in much older subjects; the tremor exists in a part which is at rest and is often temporarily arrested on voluntary movement, and, even when extensive in range, is always regular. Added to this the mask-like face, fixed attitude, festinating character of the gait and tendency to propulsion or retropulsion are all very different to what obtains in disseminated sclerosis. On the other hand, optic atrophy, marked nystagmus, paralysis of cranial nerves, and early affection of the sphincters are foreign to the clinical picture of paralysis agitans. Moreover, ankle-clonus and the extensor type of

plantar reflex are much less likely to occur, especially as early phenomena, in the course of the disease.

*Tabes.*—The class of case of this affection likely to be confounded with disseminated sclerosis is that in which motor weakness preponderates and ataxia is slight. Failure of the pupil to respond to light is rare in disseminated sclerosis, and, if present, would probably be associated with other evidences of implication of the brain by the disease; whereas in tabes it may be the only indication of the kind. Moreover, cases of disseminated sclerosis in which the knee-jerks are abolished are not common, and, when met with, may reveal the extensor type of plantar reflex which does not form part of the clinical picture of uncomplicated tabes. Besides this, the knee-jerks may be absent for a time and then return; whereas in tabes, after being really abolished, they do not return except where degeneration of the pyramidal tract has subsequently occurred, as in a case recorded by Drs. Hughlings Jackson and James Taylor, or, as I have seen, after a course of mercurial innunction. Wassermann's reaction for syphilis or cytological examination of the cerebrospinal fluid obtained by lumbar puncture may further aid in the diagnosis of tabes as opposed to disseminated sclerosis.

*Subacute Combined Degeneration.*—This affection, though resembling disseminated sclerosis in some of its features, presents many points of difference. It attacks people past the middle period of life, and progresses without remissions to a fatal termination in a few years, or it may be a few months. The cranial nerves, including those to the ocular muscles, are usually unaffected and, although the eyes may be a little unsteady on movement, definite nystagmus does not occur. The discs are normal, and there is no affection of vision. Gross defect of sensibility of the segmental type occurs in the later stages, and the sphincters do not become affected until much later in the course of the malady than in disseminated sclerosis, though they are then usually severely paralysed. A characteristic feature of the disease is the way in which spastic paralysis with exaggeration of the tendon-jerks may be rapidly replaced in the later stages by flaccid hypotonic condition of the muscles with abolition of the tendon-jerks. Moreover, the patients commonly become profoundly anaemic, and die in a state of profound wasting and septic intoxication.

*Motor Neuron Disease.*—The variety of motor neuron disease, formerly known as amyotrophic lateral sclerosis, must be considered, for whether the manifestations be limited to the spinal cord, or involve the bulb, the question of diagnosis from disseminated sclerosis in which atrophy of muscles is present may arise. The distinguishing feature is that in disseminated sclerosis paralysis precedes muscular atrophy, whilst in amyotrophic lateral sclerosis atrophy precedes paralysis, and the latter is proportional to the degree of atrophy.

*Syringomyelia.*—The class of case of disseminated sclerosis last considered may similarly suggest syringomyelia, the more so as nystagmus may exist in both diseases; but the trophic disturbances of the skin and

perhaps of the joints, preservation of tactile sensibility with abolition of the power of perception of painful and thermal impressions, together with the presence of lateral curvature, do not, as a rule, leave the diagnosis long in doubt.

*General paralysis of the insane* and disseminated sclerosis may resemble each other closely in some cases. Mental changes may occur in both; but dementia is present only in advanced stages of disseminated sclerosis, and is never so marked as in general paralysis; and though there may be a condition of bonhomie, there is never anything amounting to the grandiose state met with in a good many subjects of general paralysis. The resemblance of the speech-defect is superficial, and on careful examination the differences are easy to distinguish. The paralytic speech is tremulous, but not scanning; and paraphasia literalis does not occur in disseminated sclerosis.

Although in general paralysis there may be intention-tremor, which may be very difficult to distinguish from that of multiple sclerosis, as a rule there is no such difficulty, as it is more of a fibrillar tremor, affecting especially the facial muscles and tongue; and even when of greater range of oscillation, the vibrations can be distinguished by their constant presence, irrespective of voluntary movement.

In spite of the attempt of Moncorvo and others to establish a connexion between syphilis and disseminated sclerosis, an antecedent history of the former disease would lend weight to the opinion that the disorder of the nervous system was general paralysis rather than disseminated sclerosis, so that as much reliance is to be placed on Wassermann's reaction and cytodiagnosis as in tabes.

*Cerebrospinal syphilis* may give rise to very similar symptoms; especially to optic nerve changes, spastic paralysis, and apoplectic attacks. But nystagmus, tremor, and scanning speech are wanting; whereas in disseminated sclerosis the sensory phenomena are in the background, and there are usually no meningitic symptoms: dementia is less common, as are also paralysis of cranial nerves and hemiplegia. Assistance may be obtained by testing the effect of antisyphilitic treatment, but this is not decisive, as some cases of disseminated sclerosis may improve, although the disease is not due to syphilis. Far more reliance is therefore to be placed on Wassermann's serum test and the results of cytodiagnosis, as in tabes and general paralysis.

*Cerebral Tumour.*—Mistakes in diagnosis may be made in the class of cases of multiple sclerosis in which hemiplegia occurs, it may be, with headache, optic neuritis, and other symptoms of apparent cerebral origin. Or the mistake may arise through ignorance of the fact that a tumour, especially if situated in the pons or crura, may give rise to an inco-ordination of movement closely resembling that seen in disseminated sclerosis, and occurring only on voluntary movement; and that nystagmus and inco-ordination may be indications of a tumour seated in the cerebellum. On the other hand, it must be borne in mind that a sclerotic patch involving the cerebellum, or one of its peduncles, may give rise to symptoms



resembling those of tumour; although optic neuritis is usually absent and pressure-symptoms would of course not occur.

Although optic neuritis may occur rarely in disseminated sclerosis, it does not usually assume the form of choked disc; and there is an absence of evidence of increased intracranial pressure as revealed by slow pulse, vomiting, and so on. Where it is not possible to arrive at a diagnosis, spinal puncture has been suggested as an aid, since increase of cerebro-spinal fluid would not be expected in disseminated sclerosis; but it is only where the symptoms suggest a tumour so situated as to be accessible to surgical interference that such a method of diagnosis seems justified. (For the diagnosis from tumour of the spinal cord, *vide* p. 875.)

*Apoplexy.*—As apoplectiform attacks sometimes occur in multiple sclerosis it becomes necessary to distinguish such attacks from the results of the rupture of a cerebral vessel or its occlusion. Such attacks in disseminated sclerosis are always transitory, and no evidences of descending degeneration appear. Further, the premonitory symptoms of true apoplexy are wanting, and there is an absence of the initial fall of temperature which accompanies the commencement of the attack.

*Birth Palsies.*—Affections of this kind, in which the motor cortex of both cerebral hemispheres are involved, may be responsible for inco-ordination of movements of both arms and legs indistinguishable from the jerky movements of multiple sclerosis; furthermore there may be a closely similar defect of speech. The history as a rule suffices to distinguish these cases; but when it cannot be obtained satisfactorily some uncertainty may exist for a time. The progress of the two affections is so totally different that it cannot be necessary to extend the observations over any long period of time before arriving at a definite diagnosis.

*Toxic Tremors.*—There is little likelihood of any real difficulty in diagnosis arising in this connexion. In some cases of chronic alcoholism, in addition to tremor there may be nystagmus-like twitchings of the eye-balls. The tremor is fine and rapid, and affects the tongue as well as the hands; moreover, it may be aggravated by cutting off stimulants, and diminished by their administration.

Mercurial tremor persists apart from voluntary movement; and in cases in which it occurs the patient is already in an advanced state of cachexia which cannot be mistaken. In addition to this, both in alcoholism and in mercurial poisoning, other symptoms which characterise the existence of disseminated sclerosis are absent.

*Prognosis.*—As soon as we have established our diagnosis a fatal prognosis appears to become equally certain; but in few diseases is it more difficult to fix the probable duration of life with approximate certainty. All observers, however, do not take so hopeless a view of the affection; von Leyden is supported by Nespor in his belief that cure is sometimes possible in young people. We have noted the great tendency in this disease to apparent recovery, or considerable amelioration for long periods. It is obvious, therefore, how hazardous it would be to express

too confident a prognosis when we are able to recognise the disease early. If the case is seen after one or two periods of apparent arrest or improvement, life is likely to be spared longer than in the case of a more or less steady progress without material remission; but there are many notable exceptions to this rule; and, as already quoted, Charcot considered that patients in whom "spinal" symptoms only are present may live for twenty years or more. Symptoms indicating implication of structures in the medulla are of grave import, and may be taken to mean that a fatal issue may be expected much earlier than when such symptoms are not present.

The degree of care and attention that can be obtained in the way of good nursing materially affects the prognosis as regards the probable duration of life; more especially where there is a tendency to trophic disturbance of the skin, loss of control over the sphincters, or retention of urine requiring the use of the catheter. Irrespective of the care that can be given in the nursing of the patient, the early occurrence of bladder troubles is an indication that the duration of life will be shorter than other manifestations of the disease would justify us in supposing; for in spite of all care that may be exercised in the nursing of such cases the risks of cystitis and secondary pyonephrosis are great.

**Treatment.**—The therapeutic prospects in disseminated sclerosis are gloomy in the extreme; no medicinal agent has the slightest effect in arresting the disease or in retarding its progress. Various remedial agents have from time to time been vaunted, some no doubt in consequence of erroneous diagnosis in the first instance, and others in ignorance of the remissions which are common in the course of this disease.

The drugs to which we are justified in giving a fair trial are silver and arsenic. The former drug may be given with advantage, either as the nitrate or in the form of the chloride, in increasing doses by subcutaneous injection. Eulenburg has recommended that arsenic also should be similarly administered; but it is doubtful if this mode of giving the latter drug has any advantages over its oral administration.

According to Grasset, solanin diminishes the amount of tremor, but it has been suggested by Collins that where this drug has appeared to do good the diagnosis was at fault, the cases in reality having been hysteria. Contrary to Oppenheim's experience I am satisfied that many cases improve under inunction of mercury, provided this treatment is combined with a great deal of physical rest and a liberal diet modelled on the lines adopted in a "rest cure." The results obtained by intramuscular injection of fibrolysin in this and other sclerotic affections of the nervous system have not been such as to justify our recommending this mode of treatment, and my own experience of the use of fibrolysin in these affections has been disappointing. Hydropathic and electrical treatment, both of which have been recommended more especially by German authorities, have failed to give satisfactory results in the hands of competent physicians. These measures should, however, have

a fair trial in the earlier stages of this affection; and massage, with passive movements at the various joints, is of undoubted value in lessening the tendency to permanent contracture and to spasmodic rigidity.

But, although we can do so little to influence the morbid process directly, we can do much indirectly to retard the progress of the disease, and to make the time that remains to the patient a great deal more endurable than it would be without skilled medical aid and careful nursing. In the first place, it has been found that these patients, in the northern parts of the globe, are less comfortable in winter than in summer; so that, where it is possible, they should be sent to spend the winter months in warm climates. All depressing influences must be removed as far as possible; rest must be secured; and every means taken to maintain the general health at as high a standard as possible by open-air carriage or wheel-chair exercise, the administration of nutritious food, cod-liver oil and malt, medicinal tonics, and the like. In female patients pregnancy is especially to be avoided; for during the latter half of pregnancy, and it may be after delivery, the disease is more likely to advance rapidly. Fatigue of all kind, both physical and mental, must be avoided; as must indulgence in wine and venery.

The occurrence of bed-sores, cystitis, and similar complications call for the generally recognised means for their alleviation which will be found described in other parts of this work (*e.g.* Vol. I. p. 135). Intercurrent affections must be treated on general lines if they occur in the course of the disease.

The time has not yet arrived when we can speak with any degree of certainty or confidence with regard to preventive treatment in this disease; but many facts in the etiology at any rate warrant our insisting on certain points in this respect, and in the hope that a not very distant future may bring us face to face with a rational and more hopeful means of dealing with so intractable a disease.

The infectious fevers appear to play so important a part in the causation of disseminated sclerosis, that it is incumbent on us to enjoin a sufficiently long period of rest and other means of recuperation after such illnesses; more especially when symptoms indicating derangement of the nervous system, no matter how slight in degree, have been observed during or after the acute disease. Similarly, means should be adopted to reduce to a minimum the chances of intoxication in the various trades in which metallic poisons are used.

All-important is it that we should warn those who have had initial manifestations of what may prove to be disseminated sclerosis, to take every care of themselves; to maintain their nutrition at a high standard; and especially to avoid depressing mental and physical influences, injury, exposure to wet and cold, and excesses of all kinds. I have said that women suffering from the disease should be emphatically warned against pregnancy.

PSEUDOSCLEROSIS.—In 1883 Westphal published 2 cases in which



the symptom-group of disseminated sclerosis was present during life, but in which no corresponding changes were found after death.

One of the cases was that of a young man, whose illness began at the age of eighteen years with weakness of the upper and lower extremities, and double vision; death resulted nine years later, before which time the following symptoms became manifest: weakness of intellect; speech which was nasal without being quite scanning, and which finally became quite unintelligible; tremor of the head, lower jaw, muscles about the mouth and tongue; slowness of all movements; marked tremor of the arms on movement; and stiffness and uncertainty in the legs. The tendon-jerks were active, sensibility was normal, as were the sphincters also; and the act of swallowing remained good up to the last. On necropsy, the brain, besides being anaemic, was very hard, especially in its posterior parts; otherwise nothing abnormal was found either on macroscopic or microscopic examination. No sclerotic patches and no tract affection.

The second case was also in a male subject. At the age of thirty years, soon after an attack of enteric fever, he became weak in his legs, and had a dead feeling in his hands. The progress was slow, but in time distinct physical disturbance became evident: speech became difficult and altered, often scanning; there was marked tremor of the arms and legs, with stiffness of the latter and a spastic gait. The tendon-jerks were increased, and there was marked paradoxical contraction. Apoplectiform attacks with hemiplegic phenomena occurred, and in the course of the affection there were improvements and relapses. At times pain was complained of in the extremities, and there was slight disturbance of sensibility. There was no marked bladder trouble. Death occurred after an illness of ten years. Nothing was found at the necropsy to account for the clinical manifestations, and subsequent microscopical examination proved equally negative.

Westphal regarded as characteristic of the condition, for which he proposed the name "pseudosclerosis":—the speech-defect; the slowness of movements in the eye and face muscles, combined with a peculiar fixed expression; the physical disturbances; the apoplectiform attacks; the marked tremor in the extremities and the spastic phenomena, notably the increased tendon-jerks; the paradoxical contraction; the motor weakness; the slightness of the disturbance of sensibility, and the normal state of the sphincters.

Strümpell has recorded 2 cases which closely resemble those published by Westphal. In the first of these, during the whole of the time that the patient was under observation, the diagnosis could never be quite certain. It seemed clear, however, that some severe organic affection must be present to account for the manifestations, the most likely condition appeared to be disseminated sclerosis, as there were marked scanning speech, great intention-tremor of the arms, and spastic phenomena in the legs. This diagnosis seemed the more probable when, later in the course of the illness, apoplectiform and epileptiform attacks occurred. Yet Strümpell was never quite satisfied with the diagnosis of disseminated sclerosis, and considers that the following points militated against it: the manifestations of the disease began as early as the

age of twelve years, whereas, according to him, nearly all the cases of supposed disseminated sclerosis in children are open to question. The character of the disturbance of movement of the arms was not that usually seen with the intention-tremor of disseminated sclerosis; and in the legs the spastic phenomena were not associated with ataxia, as is observed at any rate in most cases of disseminated sclerosis. On necropsy all that was found was slight degeneration of the crossed pyramidal tracts in the cervical region of the cord, and a small symmetrical patch of degeneration on the two sides in the upper cervical cord in the region of Gowers' tract, which areas of degeneration could be traced to the lower end of the medulla oblongata. Not a single sclerotic patch was found to support the diagnosis that seemed probable. The clinical manifestations met with in Strümpell's second case also made it probable that disseminated sclerosis was the underlying pathological condition; but at the necropsy nothing abnormal was found, except that the white matter of the brain was abnormally firm, especially in the occipital region where it was quite leathery in consistence. On subsequent microscopical examination a very slight degree of degeneration of the crossed pyramidal tracts in the upper part of the cord was met with, as in his other case. Microscopical examination of the apparently sclerotic part of the brain proved that the nerve-fibres were intact, and that there was no increase of interstitial tissue.

Marie has regarded Westphal's cases as instances of hysteria; but in this opinion he receives no support either from Oppenheim or Strümpell, and the latter observer, who is, of course, quite familiar with those cases of hysteria which resemble disseminated sclerosis in their manifestations, could find nothing in the description of Westphal's cases, or in his own, to justify the assumption that hysteria was in any way concerned in the cases.

A consideration of Westphal's cases alone makes it seem possible that they depended on some form of intoxication acting on the nerves with sufficient intensity to derange function without leading to structural change; or that cruder methods of examination permitted structural changes to escape notice, which by modern methods of examination would have been detected.

The slight degenerative changes met with in the crossed pyramidal tracts in the cervical region of the spinal cord in Strümpell's cases certainly cannot be regarded as adequate to account for such severe disturbances of nerve function as were present in both cases during life.

Some important light has been thrown on the possible nature and etiology of this class of case by the changes in a third case which Strümpell included in his paper. In this, as in the other two cases, the most probable diagnosis seemed to be disseminated sclerosis, whilst at the same time there was a great resemblance between the case and those of pseudosclerosis, both in regard to the clinical manifestations and the anatomical changes. There was a complete absence of any distinct sclerotic patches such as are found in disseminated sclerosis; instead

of this the greater part of the brain was uniformly firm and leathery in consistence, just as was met with in a more circumscribed area in the two other cases of pseudosclerosis. No increase of interstitial tissue could be found to account for the increase of consistence. In the spinal cord slight but distinct degeneration of the crossed pyramidal tracts could be traced down to the lumbar region. This brings the cases of pseudosclerosis more into line with the diffuse cerebral sclerosis of which in children, according to the investigations of Goughofner, hereditary syphilis is probably a cause. Strümpell thinks that this is very likely, and sees no reason why acquired syphilis should not be operative in the cases of diffuse cerebral sclerosis that occur later in life. This would explain why so many of the manifestations of the condition resemble those of general paralysis of the insane. Moreover, according to Strümpell, it is possible that other noxious influences, such as alcohol, for instance, may be equally effective.

Important as are these cases of pseudosclerosis, they have not been met with often enough to form a serious obstacle in the diagnosis of disseminated sclerosis.

J. S. RISIEN RUSSELL.

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## SYRINGOMYELIA

SYNONYM.—*Gliosis spinalis*.

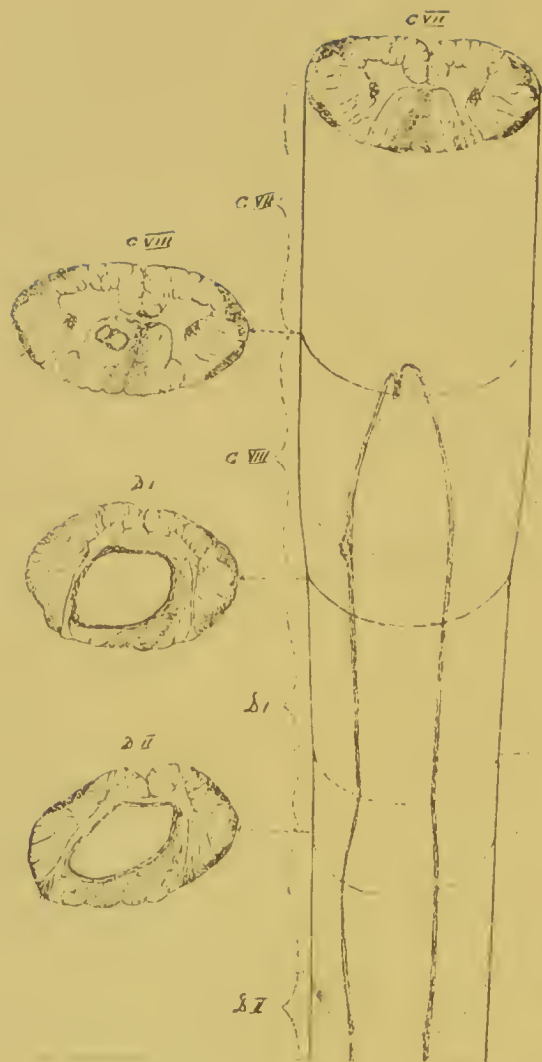
By M. ALLEN STARR, M.D., LL.D., Sc.D.

**History.**—Syringomyelia (σὺριγξ, tube; μυελός, marrow) is a disease of the spinal cord characterised by the production of a cavity of varying length within the cord. The name was given by Ollivier in 1824; but the condition was first described by Etienne in 1546, and is mentioned by numerous writers on anatomy from that time onward. Portal (1804) was probably the first to ascribe a form of spinal paralysis to this lesion, on the basis of four cases which he observed. From his time, however, until 1860 the condition, though occasionally noted by pathologists, did not excite any interest. Then with the beginning of pathological study of the nervous system various hypotheses were proposed to explain the existence of cavities within the cord, and Lockhart Clarke, Vulpian, Hallopeau, Charcot and Joffroy, v. Leyden, Schultze (31), and Kahler (14) made important contributions to the subject. In the monographs of Roth, Wichmann, and Anna Bäumlér (1889), over 100 cases with necropsies were collected and analysed. The study of these cases from a pathological standpoint was soon followed by their analysis from the clinical; and in 1887 Schultze (32) and Kahler (15) established the possibility of diagnosing this condition during life. Their statements have been confirmed by clinical observers all over the world. In Schlesinger's monograph references to 260 cases are given (29).

**Morbid Anatomy.**—The post-mortem appearances in a case of syringomyelia are very characteristic. The spinal meninges are normal. The contour of the cord is sometimes irregular, owing to a bulging at some







places, or a retraction at others; or it appears at places flattened and very small: sometimes it is not altered. Fluctuation may be detected by palpation. Usually a rupture occurs in the process of removal of the cord, and the fluid, a clear serum, runs out, leaving the cord partly collapsed. It is then evident that there is a long cavity within the cord, usually near the central canal, but sometimes so extensive as, in a cross section, to leave merely a thin ring or wall of cord tissue. Sections of the cord at various levels will demonstrate that this cavity extends for some distance through the cord, and that it varies in size and shape at different levels. The usual situation of the cavity is in the lower cervical and dorsal regions. In some cases it is short, not involving more than five or six segments; in others it is long, extending through the entire length of the cord and upward into the medulla and pons. Sometimes two or three separate cavities have been found at different levels. All possible variations have been observed in different cases. In some cases a tumour has been found on one side or within the wall of the cavity, as shewn in Plate VII.

When the cord is hardened, cut, stained, and examined microscopically, it presents certain characteristic appearances. The cavity may be of any size or of any shape, but lies chiefly near the central canal behind the anterior commissure, or in the posterior central grey matter, or in a posterior horn, or in both horns of the cord. In some cases it invades the central grey matter and the anterior horn or horns, but it is rarely symmetrical in its invasion of the cord tissue on the two sides. In some cases the place of the grey matter is entirely taken by the cavity; in other cases the cavity has invaded the white columns of one or both sides. The posterior columns are more frequently invaded than the lateral or anterior. In the most extreme cases it appears as if all the cord tissue had been destroyed; the cavity is then surrounded by a thin wall forming its sac, and no trace of grey or white substance remains. The wall of the cavity is smooth, but here and there bears papillary projections.

The cavity is usually surrounded by a zone of thick neuroglial tissue which stains deeply with carmine and haematoxylin, is unstained by the Weigert haematoxylin stain, is deeply stained by the Weigert neuroglia stain, and by the Golgi stains. The thickness of this neuroglial wall varies in different cases. Its structure is more dense near the cavity; but it is thinner in the adjacent parts, and fades away into the normal cord, usually not having a sharp boundary. Under a high power of the microscope it is seen to be made up of fine fibres, of nuclei, and of small and large neuroglial cells, a few of which are seen, in some cases, to be in a state of vacuolisation and progressive liquefaction, and to be breaking down. A fine filamentous network, containing spider-cells and spindle-shaped cells with long processes and many nuclei, extends outwards into the nerve-tissue—the appearance being that of a partial infiltration of the normal cord by gliomatous elements, the degree of which is greatest near the wall of the cavity. Such an infiltration of the cord with cells is also found in the segments above and below the limits of the cavity,

especially about the central canal. The cavity frequently occupies the place usually taken by the central canal. Sometimes it is seen to communicate with the remains of the central canal, when some epithelial elements may be found in its wall. In other cases the canal is pushed to one side and lies in the wall of the cavity. In a few sections there may appear to be two cavities side by side; but a careful examination of

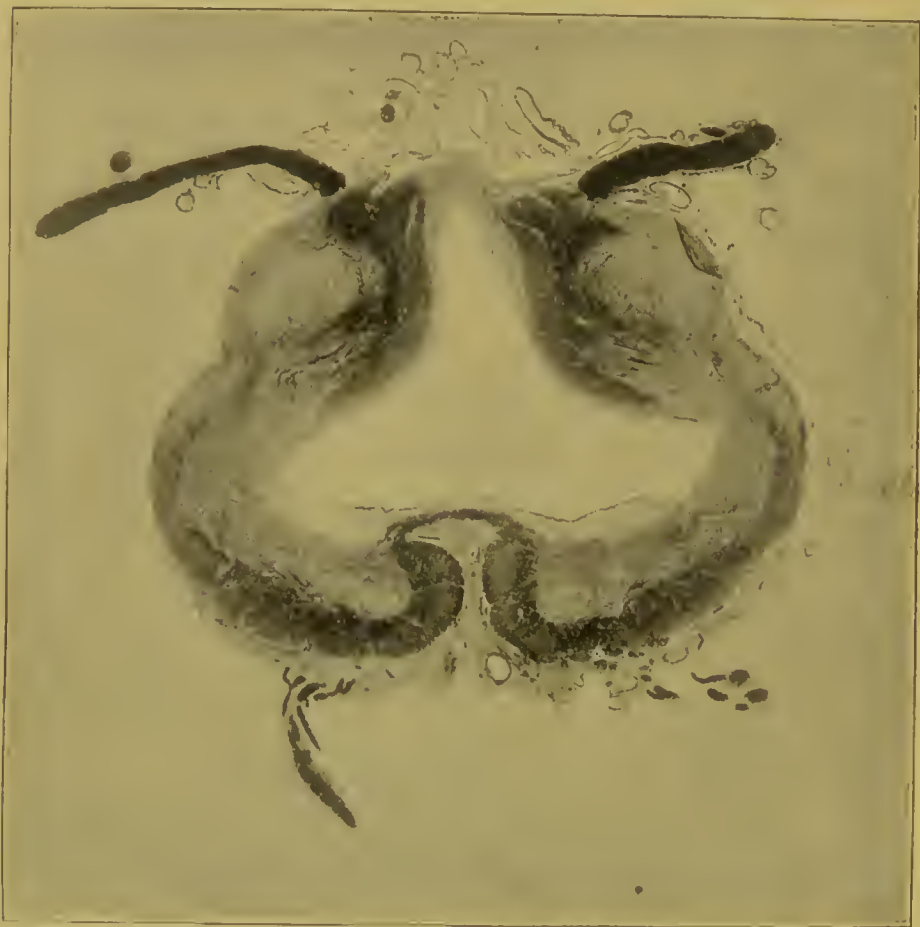


FIG. 95.—Transverse section of the spinal cord in a case of syringomyelia; first dorsal segment.

sections above or below will shew that one of these is really a diverticulum from the main cavity. The cavity itself is never entirely lined with cylindrical epithelium; but in a few cases one side of it was so lined, and in these there was a manifest opening of the original central canal into the new cavity, with more or less proliferation of the lining epithelium. A few cases have been described in which a true glioma or sarcoma filled in the cavity, being an evident outgrowth from its wall (35). Changes in the blood-vessels of the cord are sometimes observed. Very few capillaries are to be seen in the wall of the cavity; but outside it, in



the adjacent parts of the cord where the infiltration of small cells and nuclei is seen, the vessels are more numerous than normal, their calibre

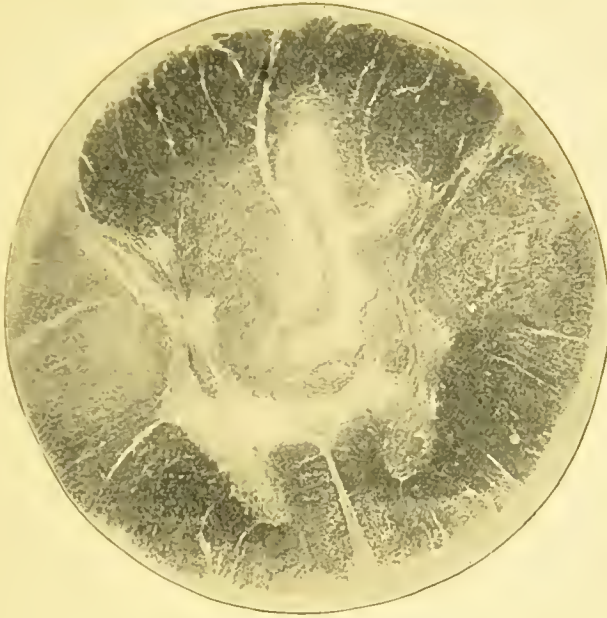


FIG. 96.—Transverse section of the spinal cord in syringomyelia; lower thoracic region. (From *Brain*, 1896, xix. 332 (Turner and Macintosh).)

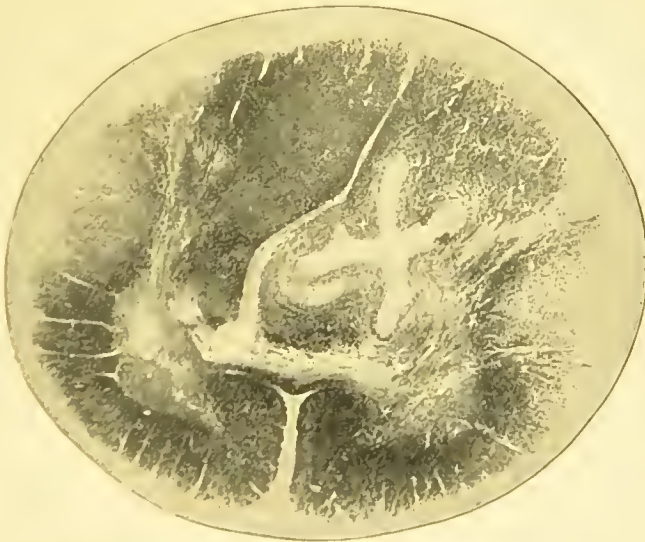


FIG. 97.—Lumbar enlargement. (From *Brain*, 1896, xix. 332 (Turner and Mackintosh).)

is larger, and they are more tortuous than usual. In some cases distinct thickening of their walls has been noticed. Capillary haemorrhages are often found within the gliomatous structure.

**Pathogenesis.**—Various hypotheses have been proposed to explain the conditions described. They may be briefly summarised as follows:—

1. It has been supposed that syringomyelia always originates in a congenital defect in the development of the spinal cord. It has been thought that during fetal life and early infancy the central canal of the cord may be unduly distended by fluid, thus remaining as an unusually large cavity within the cord, around which cavity there is a subsequent proliferation of the embryonic epiblastic elements, or a thickening of the normal glial tissue, which is known to be more abundant in this situation than elsewhere in the cord. Such a cavity is lined with epithelium, and is recognised by many pathologists under the name of “hydromyelus.” But some believe that hydromyelus may pass into syringomyelia, by the proliferation of glial cells, the invasion of the normal tissue, and its subsequent breaking down. Thus they explain the admitted fact that the degree in which the cavity in syringomyelia is lined by cylindrical epithelium is variable. Others hold that in the closure of the central canal during embryonic development a portion of it is shut off from the main canal so as to leave a subsidiary canal in the posterior septum of the cord, lined with epithelium, and surrounded, as is the normal central canal, by epiblastic tissue which subsequently proliferates, constituting a neuroglial hyperplasia, and then breaks down. Those who hold this opinion, therefore, ascribe all cases of syringomyelia to a congenital malformation of the cord, and believe that the cavity of syringomyelia has a necessary relation to the normal central canal, and usually communicates with it.

2. Another view of the disease is that the normal glial structure of the spinal cord, which is most thick about the central canal, undergoes a proliferation from some unknown cause—possibly an irritant poison in the fluid of the central canal (1); that this gliomatous new structure extends outward into the adjacent tissue, both into the grey and white matter, and subsequently breaks down in its centre, the cells becoming liquefied and disintegrated; thus a cavity originates within a gliomatous mass. This cavity at its origin has no necessary relation to the central canal; but inasmuch as the gliomatous proliferation begins, as a rule, near to the canal, the cavity usually breaks into the central canal, and thus makes a communication with it. The wall of the cavity is described as consisting of hyperplastic neuroglia with larger and smaller branching neuroglial cells, and small spheroidal cells and oval cells lying in a network of fibres, at places closely packed together, at places loosely arranged; so that it has a porous meshwork structure. This forms a sort of limiting membrane for the cavity, but beyond it within the nervous tissue there is an infiltration of glial cells. These cells are seen to be in a state of liquefactive degeneration both in the wall of the cavity and elsewhere. In some cells the nucleus is attached to or surrounded by the homogeneous remains of the cell body. Some cells are converted into sacs of fluid. Thus there is a manifest tendency in the glial cells to break down, and the cavity is the result of such disintegration. Those who hold this opinion

have named the disease spinal gliosis, believing the glial proliferation to be the essential factor in the pathology. Some of these writers consider this an inflammatory process (20); others deny anything more than a simple hyperplasia (2).

Investigations of Weigert (37) upon the structure of neuroglia seem to establish that new formations of glia may be either cellular or fibrous in structure. If cellular, the new formation is a true glioma, such as is found in tumours of the brain or spinal cord; and in such a glioma fibres are few. Weigert calls attention to the fact that this is not the structure of the glial tissue about the cavity of syringomyelia, but that the neuroglia found around this cavity consists almost exclusively of glial fibres with few cells; and that these fibres, though extending in all directions, are chiefly vertical in their course. Miura also has shewn the sharp contrast between ordinary glioma, even glioma containing a cavity, and the gliomatous condition of the cord in syringomyelia. Weigert holds that the neuroglia is merely a substance produced by nature to take the place of the nerve-tissue which has been destroyed, and that its proliferation is always a sign that the nerve-tissue has primarily disintegrated. Such destruction of nerve-tissue would therefore, according to his view, precede the formation of gliomatous tissue; hence he wholly discards the hypothesis of syringomyelia to which the name spinal gliosis has been applied. Weigert says, "Many authors believe that the essential lesion in syringomyelia is the formation of a tumour followed by softening and the formation of a cavity. It is admitted that there is a growth of neuroglia of the typical fibre-type about the cavity. But this fibre mass, devoid of cells, does not resemble a glioma, and there is no reason to believe from the mere presence of neuroglia that the cavity is not a congenital or acquired abnormality of the central canal. There is a thick cluster of neuroglial fibres normally about the canal. By the pressure in this enlarged canal the nervous tissue may be destroyed, and hence a growth of neuroglia fostered. If the pressure increases, the neuroglia may also be destroyed, and in its place about the cavity a hyaline formless mass may remain. The gliosis is not the essential feature, it is only a secondary result" (38). A case, however, has been described in which there was a gradual and direct transition between a true glioma and a gliomatous infiltration of the cord with the production of a cavity (35).

3. Many authors have observed, subsequently to disease of the spinal arteries, the formation of cavities in the cord, in their situation independent of the central canal. Thus, Müller and Medin have seen a cavity in the grey matter of the cord with walls of normal nerve-tissue, with no signs of inflammatory disease or of proliferation in the glia; the size of the cavity corresponding in situation to the degree of endarteritis in the spinal vessels, and having no definite relation to the central canal. Wieting has described a cord containing numerous cavities due entirely to the low nutrition and consequent necrosis of the nerve-tissues from disease of the spinal arteries in connexion with meningo-myelitis. It has been thought by Kronthal that lymph-stasis within the cord, and consequent necrosis



produced by transverse compression of the cord, may lead to the formation of cavities which may or may not communicate with the central canal; but this surmise is doubtful, since compression by tumours, or after Pott's disease, is not found to cause cavities. The supposition that a cavity in the cord may be due to a morbid condition of the blood-vessels seems proved for some cases; but such cavities do not resemble those of syringomyelia, and the suggestion finds little support in Weigert's hypothesis regarding the function of neuroglia. For if this hypothesis be correct, a neuroglial growth would occur to take the place of the disintegrated nerve-tissue, and in the attempt of Nature to fill up the empty space would be thickest about the cavity. Necrotic cavities, however, rarely have a well-marked wall.

4. Van Gieson described a condition, which he calls haemato-myeloporosis, of perforating haemorrhage in the cord, with the production of a long, narrow cavity. Such a cavity is occasionally surrounded by thickened glial tissue. Van Gieson shewed that some cases which have been described as syringomyelia have really been cases of old haemorrhage. Drs. Turner and Mackintosh point out that the presence of a fibrin-like material, which they describe in some of the cavities in several cases of gliomatosis of the cord, suggests that haemorrhage assists in the formation of these spaces. P. Bailey has shewn that in cases of spinal injury small haemorrhages may occur within the grey matter of the cord, and these tend to perforate the cord upwards and downwards, forming a pencil-shaped clot. The destruction of the grey matter produces symptoms identical with those of syringomyelia; and the gradual shrinkage of the clot and its absorption with the formation of a limiting layer of connective tissue about it finally causes a pathological appearance quite similar to that described as syringomyelia. It is probable that cases diagnosed as syringomyelia developing acutely, or after injury, are of haemorrhagic origin.

It seems evident, therefore, from a review of these various hypotheses, that cavities may be formed within the spinal cord in varying circumstances, and by various pathological processes. First, from congenital defects of development; secondly, by a disintegration subsequent to a neuroglial proliferation, either of inflammatory origin or of spontaneous occurrence; thirdly, as the result of retrograde metamorphosis of tissue, the nutrition of which is impaired by obstruction to the circulation; fourthly, by actual destruction of the cord by haemorrhage.

Lastly, there is not wanting a hypothesis which would trace it to bacteriological infection. Prus, from careful study of Morvan's disease, reaches the conclusion, which several authors had already announced, that Morvan's disease and syringomyelia are identical. He points out, however, that Zambaco declared Morvan's disease to be identical with lepra anaesthetica. And he appears to be willing to admit that the three diseases are, in fact, due to the same cause, namely, an infection of the nervous system by a germ which, in the slighter forms, attacks the peripheral nerves only, and in the more severe forms attacks the spinal

cord. In this view the neuroglial formation is set up by the irritation of the bacillus, and the cavity is due to the disintegration of the gliomatous substance. This hypothesis is strongly combated by Babes, who has observed 6 cases of leprosy in which the bacilli were found in the cells of the cord, but in which there was no lesion resembling that of syringomyelia. The time has not yet come to establish conclusively any one of these views of the origin of syringomyelia. In fact, until cases are observed at the onset of the disease, as well as after a long duration, no basis for a conclusion can be established.

When the cavity has existed for some time it is not uncommon to find evidences of ascending and descending degeneration in the columns of the cord, which are secondary either to pressure, or to the destruction of tissue at its point of maximum extent. Degeneration in the motor nerves and atrophy of the muscle-fibres are also parts of the lesion in this disease. The various trophic disturbances in the bones and skin also require mention (*vide* pp. 85, 103).

**Symptoms.**—The diagnosis of syringomyelia rests upon the presence of three characteristic symptoms which, in the majority of cases, are present together. The existence of one of these symptoms alone should excite suspicion of the possibility of the disease being present; the presence of any two of them makes the diagnosis very probable. These symptoms are—(i.) a loss of the sensations of pain and temperature in any part of the body, tactile sense being preserved in the analgesic area; (ii.) trophic disturbances in the skin, muscles, bones, or joints; (iii.) progressive muscular atrophy attended by paralysis.

In addition to these symptoms may appear (*a*) a spastic paraplegia, or (*b*) disturbance of tactile sense with pain, or (*c*) the general symptoms of transverse myelitis in case the disease invade respectively the (*a*) lateral, or (*β*) posterior columns of the cord, or (*γ*) its entire area. Such an extension is not uncommon, and hence these symptoms must be considered as a frequent complication. Another series of symptoms may appear if the disease invade the medulla and pons, for then signs of bulbar palsy develop.

The distribution of the characteristic symptoms of the disease will depend entirely upon the extent of the lesion in the cord. As this lesion usually begins in the cervical segments the symptoms almost always appear in the hands. If the lesion be limited to one or two segments of the cord the symptoms will be very limited; but if it extend throughout the entire length of the cord, and upward through the medulla and pons to the crus, the symptoms will be widespread and will involve the cranial nerves. The course of the disease is a very chronic one, the symptoms coming on slowly at any age, and often reaching a certain point and remaining stationary for years—the life of the patient being ended, as a rule, by some intercurrent disease; though occasionally sudden death is caused by the rupture of the cavity.

(i.) The disturbance of sensation, called by Charcot *dissociated anaesthesia*, is the chief characteristic of the disease. This symptom is

frequently unknown to the patient until it is demonstrated by the physician; although occasionally among the working classes, who are more exposed to injuries, the patient may have noticed that such injuries, especially burns, were not attended by pain. It is found upon examination of these persons, that pricking, or cutting, or burning, or freezing of the affected area is not attended by sensations of pain, or of heat or cold; though the sense of touch is preserved. The sense of heat may be impaired when that of cold remains, or conversely. The sense of pain is a great protection to the body, giving warning of injury, and assuring care and rest of the part; hence its absence exposes these patients to the risks of serious affections of the skin and joints, the consequences of neglect of small pathological processes at their start. The sense of touch is not often affected at all; although in cases in which the cavity progresses to a considerable size, and invades the posterior columns of the cord, it may become somewhat blunted. The muscular sense appears to be preserved, excepting in this last class of cases. The distribution of the analgesia in syringomyelia is usually irregular, rarely symmetrical on the two sides. Inasmuch as the affection is more common in the cervical region the condition of the analgesia is more frequently found in the hands and arms; and as it is frequently found that small injuries to the fingers are not attended by pain, this abnormality is the first to direct the patient's attention to the existence of his disease. In the early stages there is merely a decided blunting of the sensations of pain, and an inability to distinguish between slight variations of temperature; or certain sensations only are not perceived. Thus, Dejerine records a case in which the thermal sense was lost for all temperatures above 68° F. The area of analgesia may not coincide exactly with that of loss of temperature sense. Paraesthesia of temperature or sharp pains rarely precede the loss of sensations. When the disease is fully established the patient cannot distinguish between ice-cold and boiling water, and deep incisions may be made into the flesh without the slightest pain.

(ii.) *Trophic disturbances* are very frequent in syringomyelia. In the majority of the cases it is evident that the origin of these disturbances is some injury, wound, or burn which on account of the loss of pain sense had not been observed, and therefore neglected, had become infected, and had gone on to ulceration or suppuration. In some cases, however, it is impossible to ascribe trophic disturbances to such causes, and indeed the hypothesis of the existence of trophic centres in the spinal cord presiding over the general nutrition and the repair of the body receives its chief support from the facts observed in this disease. The skin is the seat of the chief trophic disturbances, which may be of various kinds. There may be localised hyperaemia or anaemia of the skin; there may be changes in the perspiration, the part being abnormally covered with sweat or abnormally dry; and, in addition to the acute inflammations of the skin already attributed to injuries, cases of serous exudation with desquamation, gangrene of the skin and subcutaneous tissue, bullae and peculiar hypertrophies and atrophies of the skin



have been observed. Another trophic disturbance, which has excited much interest, is the appearance of painless whitlows upon the fingers and of small abscesses about the extremities. Morvan described a disease occurring in a seaport among fishermen, in which whitlows appeared upon the fingers, producing deep ulceration and even necrosis of the terminal phalanges, and were associated with other trophic disturbances of the skin and nails, and with analgesia. This disease, which was at first named after Morvan, is now thought to be a variety of syringomyelia; for in all the cases examined after death a cavity has been found in the cord. The growth of the nails is commonly affected; they are hypertrophied, ridged, occasionally stained, and become particularly brittle, and irregular in their form.

Affections of the joints and bones are very frequently observed in syringomyelia. In fact, there is no nervous disease in which joint affections occur so commonly as complications. The shoulder, elbow, and wrist are the joints most commonly affected; in this respect the disease offers a contrast to tabes, in which the joint affections most frequently occur in the lower extremities. The character of the joint affections is, however, as a rule, quite similar to that described by Charcot as characteristic of the joint disease in locomotor ataxia—a large effusion within the joint with great thickening of all the tissues, and later an absorption of the bones with an atrophy of the joint surfaces. Schlesinger has collected 105 cases with joint affection occurring in the course of the disease, and he estimates that this complication occurs in more than 10 per cent of the cases. Alterations in the long bones are observed in syringomyelia; and spontaneous fractures, due to a spongy and brittle condition of the bones, have been recorded by a number of observers. The joint affections and these fractures proceed alike without pain to the patient, and hence are often neglected for some time after they begin (*vide* p. 96).

In a considerable number of cases a marked curvature of the spine, either lateral or forward, and occasionally backward, has been observed. This has been ascribed by some authors to atrophy and weakness of the spinal muscles, and by others to actual changes in the bones. Both conditions may occur. The spine is, as a rule, sensitive to pressure; and deformity is more likely to occur in the upper portion of the dorsal region than elsewhere. It is never very extensive. In a few cases the combination of acromegaly with the symptoms of syringomyelia has been observed, one of these cases having been seen at my clinic; but it is by no means certain that this combination was more than accidental. As the records of the disease have increased, its incidental association with various other diseases—hysteria, paralysis agitans—has been recorded. Such associations have no particular significance.

(iii.) *Muscular atrophy attended by paralysis* is present in more than half of the cases of syringomyelia. It usually begins as a progressive muscular atrophy invading the hands, especially the first interosseous muscle, then the thenar and hypothenar eminences, finally producing claw-hands (*main en griffe* of Duchenne), and then advancing up the limb

to the forearm, arm, and shoulder. Bieganski in 1895, and since that date Testi, Cardi, and others, have found evidence of syringomyelia in the cervical and lumbar enlargements of the cord in patients with Dupuytren's contraction of the palmar and plantar fascia. Occasionally the shoulder muscles are the first affected, and then the atrophy is distributed to the deltoid and scapular muscles, and later invades the biceps and supinator longus. The muscles of the spine are particularly liable to be invaded by the atrophy and paralysis, and as a consequence curvature of the spine is a very frequent symptom in this disease. The legs are less frequently affected (12 per cent of the cases), but atrophic paralysis of the thighs or of the legs below the knee, with consequent contractures, has been seen.

The exact distribution of the atrophy and paralysis depends upon the extent of the lesion in the various segments of the cord. In a table given on pages 637, 638, the relation between the various muscles of the body and the various segments of the cord is shewn. It is therefore evident that from the muscles invaded in any instance we may infer the extent of the lesion. The atrophic paralysis of the muscles is frequently attended by fibrillar contractions and tremors, and by a gradual diminution in the mechanical and electrical contractility of the muscle. It is not until the last stage of the disease, when the muscle is extremely atrophied, that it presents the reaction of degeneration.

(iv.) *The spinal reflexes* may be disturbed in this disease. When the symptoms are located in the arms, the elbow- and wrist-reflexes are absent, while the patella reflex is, as a rule, increased. If, however, the disease invade the lumbar region of the cord the patellar reflex may be lost on the side of the lesion.

In a few cases in which the sacral region of the cord has been diseased a loss of control of the *bladder and rectum* occurred.

(v.) The spinal centre of the cervical sympathetic nerve lies in the first dorsal segment of the cord, and, as this segment is most frequently affected, symptoms of *paralysis of the sympathetic* on one or both sides are commonly to be detected. They are a narrowing of the palpebral fissure, a retraction of the eyeball, sluggish pupillary action with imperfect dilatation, a flattening of the side of the face, and a defective secretion of sweat.

(vi.) The extension of the disease to the medulla may cause symptoms referable to the implication of *the cranial nerves*. Atrophy with fibrillar tremor in the tongue and facial muscles, ocular palsies with nystagmus, and dissociated anaesthesia of the face and head have been observed. In a few cases paralysis of the vocal cords, disturbances in the act of swallowing, difficulty of respiration, and irregular action of the heart indicate that the vagus centre is affected. These symptoms are most serious, as sudden death commonly ensues (30).

The course of the disease is a chronic one. It advances slowly sometimes after an injury, and the symptoms are well established, as a rule, before the disease is recognised. The patients remain for months in a

stationary condition, or the paralysis slowly increases until they are disabled. The symptoms may finally extend to the entire body, though this is rare. Death occurs either from extension to the medulla, or from cystitis or bed-sores, or from some intercurrent affection; in rare cases sudden death has occurred unexpectedly from a rupture of the cord allowing an escape of fluid from the cavity.

The following case under my observation at the Vanderbilt clinic illustrates the usual symptoms and course of the disease:—

P. S., of healthy parentage, noticed in March 1896, when he was sixteen years of age, that he was becoming weak and clumsy in his hands, that he was dropping things unintentionally, and was losing strength also in his arms. These symptoms were noticed in the left arm before they were in the right. They were not attended by pain or any noticeable sensory disturbance. It was noticed that his hands and arms became gradually thinner as they became weaker, and the emaciation soon extended to his body, especially about the muscles of the chest and back and scapulae. He was not aware of any sensory disturbance until the time of his first examination at the clinic in January 1897.

He had had no trouble in his bladder or rectum; nor any symptoms in his legs, excepting a slight weariness on any exertion; but he had noticed that his back had gradually become crooked, the right side of his body appearing to bulge. It was evident from the history that all his symptoms had made such gradual progress during the past year that they had not attracted much attention until his inability compelled him to leave off work.

Examination in January 1897 shewed a very well-marked condition of atrophy, with corresponding paralysis in the muscles of both upper extremities, chest, scapulae, and thorax, as shewn in Fig. 98. No muscle was entirely paralysed, but all the muscles were extremely weak; they presented fibrillar



FIG. 98.—Atrophy of the arms and muscles of the back and thorax, with lordosis, in a case of syringomyelia.



contractions on exposure to cold or on percussion, but did not shew any reaction of degeneration. The atrophy was extreme about the muscles of the scapulae and in the deltoids and upper part of the arms. The muscles of the thorax and back were markedly atrophied, so that a lordosis was very evident, causing peculiar motions of balancing in the act of walking. The atrophy was about equal on both sides. The biceps was less atrophic than the other muscles of the upper arm; the flexors and extensors of wrist and fingers, and thenar and hyperthenar muscles, and interossei of the hand were very decidedly atrophic. The lower portion of the pectoralis major on both sides was preserved, but the upper part was atrophic. The interossei and the muscles of the back were very atrophic. The muscles of the abdomen and legs were not in any way affected,

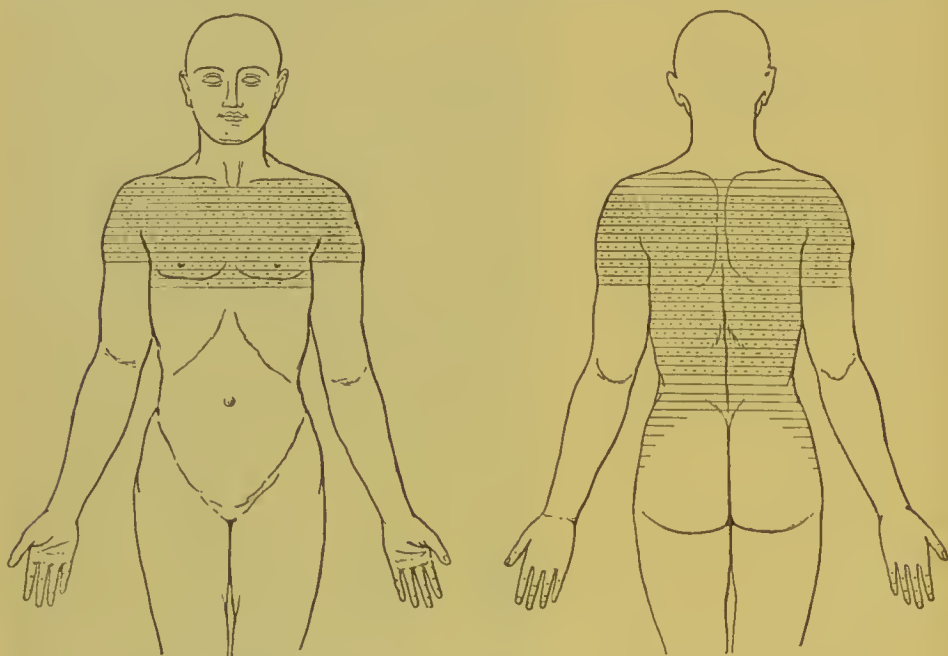


FIG. 99.—Areas of analgesia and thermo-anaesthesia in a case of syringomyelia. Lines shew area of thermo-anaesthesia; dots shew area of analgesia.

but the knee-jerks were very much exaggerated, and there was ankle-clonus on both sides. The elbow- and wrist-reflexes were lost. The face was normal. Sensation to touch was preserved in all parts of the extremities, body, and thorax; but sensation of heat and cold, and of pain, could not be elicited over the regions shewn in the diagram (Fig. 99). The loss of pain sense was somewhat less extensive than the loss of sensation to heat and cold on the back. This patient was observed very carefully in St. Luke's Hospital for six months, there being little or no change in his condition.

**Diagnosis.**—When the three characteristic symptoms already described are present in any case, there is no question regarding the diagnosis of syringomyelia. In the early stages of the disease, however, before all three symptoms appear, other spinal affections may be suspected. Thus, many cases are regarded for a considerable time as cases of

progressive muscular atrophy; and it is only on the appearance of the peculiar sensory disorder, or of the trophic symptoms in the skin or bones, that the diagnosis becomes questionable. In other cases the early suspicion may be of tabes, especially if the disease be located in the lower part of the cord; for then the pains, especially the burning sensations, the disturbances in temperature and pain sense, and the paræsthesia, with trophic disturbances in the joints and loss of tendon-reflex at the knee, may suggest tabes, even though ataxia be not manifest. Then it is only when atrophies of the muscles and paralysis concur that syringomyelia is suspected. The diagnosis from amyotrophic lateral sclerosis may be made from the fact that in this disease there is an increase of mechanical excitability in the paralysed muscles, an increase of reflex action, an early appearance of a spastic gait, an absence of sensory symptoms, and little tendency to trophic disorders.

A general myelitis or a disseminated myelitis may be diagnosed in cases of syringomyelia, when both motor and sensory and trophic disturbances are present; but the lack of symmetry of the sensory disorders and the peculiar preservation of tactile sense in syringomyelia should enable the observer to avoid this mistake. It is, however, to be remembered that in some cases the two diseases occur together (10).

Whilst it is true that syringomyelia has a close analogy to tumour formation in the spinal cord, especially to glioma, it must be remembered that tumours of the cord are usually limited in extent to two or three segments; that they produce more widespread symptoms than syringomyelia, especially in the body below the level of the lesion; that the symptoms resemble those of a transverse myelitis of rapid onset, and that in spinal tumours pain of a severe character is a constant symptom. The course of the disease, steadily progressive in tumour, may aid the diagnosis when symptoms are ambiguous. Pachymeningitis cervicalis (*vide* p. 597) may give rise to somewhat similar symptoms in the arms; but the severe pain in the neck, the rigidity and the fixed posture, the absence of dissociated anaesthesia, and the lack of trophic disturbances, will prevent any mistake in diagnosis.

Syringomyelia presents some of the features of bulbar palsy when the cavity invades the medulla and pons; but the cavity is rarely confined to the medulla and pons, and hence in syringomyelia the symptoms are not exclusively bulbar; thus is afforded a point of distinction between the two diseases. A number of cases, however, have been recorded in which the disease began in the pons and medulla, and in which, for some months, the diagnosis of bulbar paralysis was made. The course of the case, the extension of the characteristic symptoms to the arms, and the final result prove these cases to be syringomyelia beginning above and descending (Raymond).

**Prognosis.**—The prognosis as to recovery is unfavourable; but inasmuch as the disease rarely progresses beyond a certain point it cannot be considered dangerous to life.

**Treatment.**—No remedy is known which will arrest the pathological process. The symptoms are to be treated as they arise—the paralysis, for instance, as in poliomyelitis. The trophic disturbances may often be prevented by care; and, if they occur, are to be treated by rest, by mechanical appliances, or by surgical measures. The sensory loss cannot be remedied by faradic applications. It is to be remembered that the disease often comes to a spontaneous standstill, so that remedies of a constitutional kind are not to be implicitly trusted, even though they appear to arrest it.

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M. A. S.



## TUMOURS OF THE SPINAL CORD AND ITS MEMBRANES

By EDWIN BRAMWELL, M.B., F.R.C.P.

TUMOURS may grow in the substance of the spinal cord or from its investing membranes, and are known as medullary or intra-medullary, and as meningeal or extra-medullary respectively. Meningeal tumours are divisible into extra- and intra-dural according to their situation. Since the clinical features of meningeal and of medullary tumours are very similar and often indistinguishable, these two forms will be conveniently described together.

**Incidence.**—Spinal tumours, even using the term in its widest sense to include all growths which interfere with the functions of the cord, whether they arise in its substance, from the meninges, or from the vertebrae, are rare. Thus, among 35,000 necropsies at the General Hospital at Vienna, during eighteen years, Schlesinger found 104 cases only in which the spinal cord was implicated by a vertebral, meningeal, or medullary growth; Schlesinger states that tumours of the brain are six times as common as spinal growths, and vertebral tumours twice as frequent as meningeal and medullary combined. Among a large series collected from the literature by the same author, there were 217 cases of meningeal and 125 of medullary tumour, whilst both the cord and its meninges were affected in 35 instances. Among the 217 meningeal tumours, 142 were intradural, 75 extradural.

**Morbid Anatomy.**—The accompanying table compiled by Schlesinger from 390 recorded cases, and somewhat rearranged by Dr. R. T. Williamson, indicates the chief forms of tumour met with, their relative frequency and situation:—

Variety.	Intradural.			Extradural.		Single.	Multiple.	Total.
	Medullary.	Meningeal.	Both.	Meningeal.	Non-meningeal.			
Sarcoma . . .	14	53	9	17	11	80	27	107
Tubercle . . .	62	...	...	2	...	55	9	64
Echinococcus . . .	...	5	...	39	...	8	36	44
Fibroma . . .	...	20	2	5	...	15	18	33
Gumma . . .	7	4	15	2	...	19	9	28
Glioma . . .	20	...	...	...	...	20	...	20
Psammoma . . .	...	18	...	...	...	18	...	18
Myxoma . . .	...	7	...	4	...	11	...	11
Lipoma . . .	1	8	...	...	1	8	3	11
Cysticercus . . .	2	5	...	...	1	4	4	8
Glio-sarcoma . . .	...	3	4	...	...	...	7	7
Endothelioma . . .	...	5	...	1	...	4	2	6
Melano-sarcoma . . .	1	...	3	...	...	1	3	4
Neuroma . . .	4	...	...	...	...	3	1	4
Lymphangioma . . .	...	1	...	1	...	1	1	2
Cysts . . .	...	1	...	1	...	1	1	2
Cholesteatoma . . .	1	...	...	...	...	1	...	1
Uncertain . . .	13	12	2	3	...	24	6	30
	125	142	35	75	13	273	127	390

*Medullary Tumours.*—Tuberculous tumours are much the most common. Glioma, sarcoma, and gumma come next in order of frequency. Medullary growths are usually deeply situated, and in the first instance often unilateral. They evince a predilection for the cervical and lumbar enlargements (*vide* table, p. 869). Tuberculous tumours, as a rule, are solitary; in Herter's series of 25 cases the oldest patient was forty-three. Tuberculous lesions almost always coexist in the lungs or elsewhere. Glioma or glio-sarcoma may occur in association with syringomyelia; they are rarely localised and often extend throughout the cord. Cases have been described in which a glioma protruded beyond the surface of the cord, forming a prominent projection (Seiffert, Gründ); occasionally these tumours originate in the filum terminale (Lachmann, Schlesinger). Sarcoma may be primary, solitary, and localised, it is sometimes metastatic; in other cases a sarcoma arising in the membranes infiltrates the substance of the cord. Gumma, which is very rare, is usually associated with similar new formations in the meninges. All other forms of medullary tumour are extremely rare. Medullary tumours vary greatly in size; they may be microscopic or occupy the whole transverse section of the cord, producing at times a distinct enlargement of its contour.

*Meningeal tumours* may grow from the dura, arachnoid, or pia; and in the great majority of cases are primary. Sarcoma, hydatid cyst, fibroma, psammoma, and myxoma are the forms most often met with. Lipoma may be included, although it usually springs from the epidural fat. Sarcoma is generally intradural, and may be primary or secondary. Primary sarcoma is the most frequent tumour of the meninges (50), and is usually encapsulated and slow-growing. Multiple sarcomas are sometimes seen; and occasionally there is a diffuse sarcomatosis of the pia mater which surrounds the cord as a thick sheath, here and there, it may be, invading its substance and filling up in places the entire space between the dura and the cord. It sometimes extends from the filum terminale to the foramen magnum. Dr. Stanley Barnes, who has analysed 13 cases of diffuse sarcomatosis of the spinal pia mater, concludes from the distribution of the process that the condition is an expression of a sarcomatous infection conveyed from some primary growth higher up in the nervous system, which lies exposed to the cerebro-spinal fluid. Hydatid cysts are almost always multiple and commonly extradural; Dr. Colman has analysed 37 cases from the literature. Multiple fibroma may occur in association with similar growths throughout the body; the nerve-roots of the cauda equina are especially affected. Solitary fibroma and myxoma growing from the nerve-roots are relatively frequent, and are almost always intradural. Psammoma, which is a localised, slow-growing tumour within the dura, is not uncommon. Lipoma is sometimes met with; Spiller (56) has analysed 16 cases—11 were extradural, 4 intradural, and of these 1 was in the conus, 1 in the filum terminale, and 1 in the substance of the cord (F. C. Turner). Scanzoni has recorded 2 cases of multiple meningeal carcinoma, and has analysed the very rare instances in the literature. Myoma of the

meninges has been reported (W. Gowers, Pick, Spiller, and Forbes); these tumours grow from the vessels in the pia.

Meningeal tumours tend to spread up and down the vertebral canal in the direction of least resistance, lying especially on the posterior and lateral aspects of the cord where they have more room to grow. Increase in size of intradural tumours is limited by the dura which appears to form a practically impenetrable barrier, even to the more rapidly growing forms of meningeal sarcoma. The relations of meningeal tumour to the various aspects of the cord, a point of considerable practical importance to the surgeon, have been especially studied by Oustaniol; among 60 cases he found the tumour situated anteriorly in 7, antero-laterally in 7, laterally in 19, postero-laterally in 9, and posteriorly in 18.

The relative frequency of medullary and meningeal tumours at different levels of the cord is shewn in the accompanying table from Schlesinger's work, according to which it would appear that in the dorsal region meningeal tumours are four times as frequent as medullary growths, whereas in the enlargements the latter tend to preponderate:—

Situation.	Intra-medullary.	Intradural (meningeal).	Extradural.	Total.
Cervical region and cervical enlargement	44	18	8	70
Dorsal region . . . . .	16	34	32	82
Lower dorsal region and lumbar enlargement	42	26	9	77
Sacral region and cauda equina	6	21	8	35

The effects produced by the pressure of meningeal tumours upon the cord are of great practical importance. The symptoms of a total transverse lesion may be due to pressure alone, and, when this is so, even though the cord is much distorted, removal of the tumour is followed by recovery. In some cases the paralysis depends on a localised oedema or infiltration of the cord by the new growth; softening and myelitis are comparatively rare.

**Symptoms.**—In a certain proportion of cases of meningeal tumour pain in the back is the first evidence; nevertheless, the earliest manifestations are more often referable to the implication of nerve-roots by the growth. At a later date indications of progressive interference with conduction in the cord appear. For this reason two periods are often described, a first characterised by root-symptoms and sometimes known as the neuralgic stage, and a second distinguished by increasing loss of power and sensation in the limbs, the so-called paraplegic stage. In medullary tumours pain in the back is exceptional and absence of root-symptoms the rule.

Pain in the back, a prominent symptom in some cases of meningeal growth, but most exceptional in tumours of the substance of the cord, is



probably due to irritation of the membranes. The pain is almost always referred to the neighbourhood of the tumour. In some cases it is located to one side of the middle line. Slight at first in some cases and noticeable only on movement, on coughing or on sneezing, the pain is often very severe and constant from the outset, and is variously described as boring, stabbing, or burning. It may precede other symptoms by several months; indeed, in a case reported by Oppenheim (36) it was present for two and a half years before other symptoms appeared. In the later stages it is usually less severe and may even disappear.

Root-symptoms are very characteristic, and are often the earliest indication of a meningeal tumour. Pain is from its frequency of the first importance. The pain may be felt in the trunk or limbs according to the situation of the tumour. Very often confined in the first instance to one side of the body, at a later date, no doubt as a result of extension of the growth around the cord, it becomes bilateral. Sometimes localised formication, pins and needles, a dead feeling, or girdle-sensation in the region of skin supplied by the affected root or roots may accompany or take the place of pain. The pain, which at first may be present only on movement, is sometimes agonising. Variations depending on the weather may be observed. Disappearance of the pain in some instances in the later stages is no doubt due to complete destruction of the implicated root. The significance of the pain may not be appreciated until symptoms of impaired conduction in the cord appear. Absence of root-pains has exceptionally been noted in meningeal tumour (Nonne, Schultze, Boettiger, Oppenheim, E. Müller, Störsberg, Heilbrunner, Michell Clarke). In these circumstances the tumour has usually been in the dorsal region where the roots are widely separated. On the other hand, Lewandowsky and others have reported cases of medullary tumour in which severe pain was experienced. Again, pains with a radicular distribution are sometimes observed in areas supplied by roots which arise a considerable distance below the level of the tumour (Starr, Ransom, Bruns (10)). These pains may perhaps be accounted for by pressure on the conducting tracts in the cord itself. Hyperaesthesia is seldom observed in the region supplied by the affected roots, and tenderness on pressure over the nerve-trunks must be very rare if it ever occurs. Sooner or later some objective diminution of sensation may usually be detected. According to Prof. Sherrington's observations, hypaesthesia results only when more than one root is destroyed.

Implication of the anterior spinal roots is less frequent. The reason for this is obvious from what has been said regarding the common situation of meningeal tumours. An atrophic palsy with a root-distribution is nevertheless not infrequent. Localised muscular spasms and tremors have been observed. Bruns has pointed out that paralysis due to compression of the anterior roots may persist for a long time before the electrical excitability of the paralysed muscles is perceptibly reduced.

Signs of pressure on the spinal cord appear after a longer or shorter period. The earliest manifestation of this event is often some fatigue in

walking, more especially in the homolateral leg. Unilateral absence of the abdominal reflex may be noted even before this (37). In a case of Oppenheim's (36), the first evidence of pressure on the cord was relative thermanalgesia in the contralateral limb. The earliest spinal phenomena often point to a hemi-lesion of the cord, since both meningeal and medullary tumours are often, in the first instance, more or less unilaterally situated in relation to it. Brown-Séquard's paralysis, or the symptom-group due to a unilateral lesion of the cord, is characterised by motor paralysis, more or less rigidity, exaggeration of the tendon-jerks, an extensor response, and loss of the sense of position, on the side of the lesion, with loss of sensation to temperature and to painful stimuli, impairment of tactile sensation, and loss of the bone-vibration sense on the opposite side. This syndrome, though present in many cases, is, as might be expected, seldom met with in its pure form. As the pressure increases the paraplegia becomes more symmetrical. The weakness, which is at first most noticeable in the ankles, gradually extends upwards to the knees and hips; the knee- and ankle-jerks are exaggerated, while the cutaneous reflexes indicative of interference with pyramidal conduction (the signs of Babinski, Oppenheim, Bechterew, and Kurt-Mendel), ankle- and knee-clonus appear. The arms may be affected if the tumour is in the cervical region. The lower limbs gradually become more spastic until there is an extreme degree of rigidity often associated with distressing flexor spasms. Ataxia rather than paraplegia may be the prominent feature, as in a case of meningeal tumour reported by Thomayer. Some objective sensory impairment is usually present before the paraplegia becomes very well pronounced; first discernible, as a rule, about the feet, it spreads gradually upwards until it reaches the level of the root-paralysis. Many months may elapse before this stage is reached, and bladder symptoms generally appear first. Thus, precipitate micturition, with some delay in commencing the act, appears, and at a later date there may be retention with overflow-incontinence. In a case of glioma of the filum terminale reported by Lachmann the nerves to the bladder were alone involved. Precipitate micturition is sometimes seen in the earlier stages, and constipation is common. Priapism is an occasional symptom.

Prominence of one or two vertebrae immediately over the tumour is sometimes found, although the pronounced angular curvature seen in malignant disease or caries of the vertebral bodies is never attained. A minor degree of scoliosis which is very occasionally present is accounted for by weakness of the erector spinae muscles. Pressure upon the spines immediately overlying the tumour is sometimes associated with tenderness. A useful plan in testing for tenderness is to grasp each spine in turn between the finger and thumb and use lateral pressure. Occasionally there is pronounced rigidity of the muscles of the back. When the tumour is in the cervical region, the oculo-pupillary symptom-group may be present. Optic neuritis has been observed (Taylor and Collier).

As the pressure increases, the spasticity begins to diminish, the

tendon-jerks become less active, and ultimately the spastic paraplegia gives place to a flaccid palsy with absence of the deep reflexes (Bastian), and absolute anaesthesia up to the level of the lesion when conduction is completely abolished. Bed-sores and cystitis are very apt to follow. The flaccid stage may come on quite suddenly as a consequence of oedema or softening of the cord in the neighbourhood of the tumour.

**Diagnosis.**—A meningeal or medullary tumour may be suspected when the symptoms point to a localised and progressive lesion of the cord, and when no evidence of bone disease can be detected. The probabilities are very considerable when root-pains, especially if unilateral in the first instance, precede or accompany a progressive paraplegia of the Brown-Séquard type. The diagnosis, although very probable, is, however, as Bruns (7) points out, hardly ever quite certain in the absence of tumours in other organs.

It is difficult to differentiate *meningeal* from *medullary* tumours; indeed, the diagnosis may be impossible. Severe pain in the back and root-pains strongly suggest a meningeal growth, and the probability is increased when the symptoms are referable to the dorsal region (*vide* table, p. 867). According to Bruns and others the circumstance that the upper limit of the anaesthesia when once complete does not shew any tendency to ascend, is an important point in favour of an extra-medullary growth. Localised muscular cramps, due to nerve-root irritation and the sudden onset of total paraplegia, also favour a tumour of the membranes (Malaise). Motor-root symptoms, involving several segments of the cord and dissociated anaesthesia of the posterior-horn type, will suggest an intra-medullary tumour, and long duration of the symptoms points in the same direction.

The localisation of the tumour is to be accurately determined. Objective evidence of nerve-root involvement (a localised atrophic palsy, a sensory alteration of radicular distribution, or absence of individual superficial or deep reflexes) will, if present, prove a most important guide. The upper limit of the spinal anaesthesia may yield the only available data in localisation when root-symptoms are absent. Deductions based on the level of the spinal anaesthesia are only justifiable when the sensory defect is pronounced in degree and when its level is constant. In these circumstances, bearing in mind Sherrington's law, it may be assumed that the tumour involves at least one segment immediately above that to which the upper level of the sensory impairment corresponds. Pain in the back and root-pains may afford additional evidence from a consideration of the region to which they are referred. Prominence of an individual vertebral spine may prove a valuable guide. But as some inequality of the vertebral spines may be seen in health, inferences are apt to prove misleading unless the deformity is pronounced, or the spinous process in question is tender on pressure, or unless it approximately corresponds to the region of the cord to which the other symptoms point. Sir V. Horsley advocates the hypodermic injection of pilocarpine, a method he has employed for years, as useful in localising the boundary



line of defective secretion of sweat (*vide* p. 579). Finally, the level of the tumour can be determined by a comparison of all the available data, the highest limit to which the symptoms extend being taken as the position of the tumour. During life it is practically impossible to distinguish between an extra- and an intra-dural growth. The reader is referred for details regarding spinal localisation to the table to face page 575.

The differential diagnosis between tumours of the cauda equina and of the lumbo-sacral region of the cord is often very difficult. Prominence, pain, or tenderness on pressure over the second lumbar spine or below it are of great value, since the cord terminates above this level. Growths of the cauda equina are commonly accompanied by severe pains in the lower limbs, anaesthesia is almost invariably radicular, and the first symptoms and signs are almost always referable to the sacral rather than to the lumbar region of the cord.

The longitudinal extent of the growth can seldom be predicted. Some indication as to the relation of the tumour to the transverse section of the cord may possibly be derived from the order in which the symptoms appear.

Multiple tumours of the meninges may be suspected in those very rare instances in which multiple growths, notably fibromas, are present elsewhere, or when the symptoms cannot be accounted for by a single focal lesion.

The *nature of the tumour* is always doubtful unless—and this is very rarely the case since meningeal and medullary tumours are almost always primary—new growths are present in other parts of the body. Tubercle is probable when tuberculous lesions exist in other organs. The inference is not, however, infallible. Nonne, for instance, has described a case in which a progressive paraplegia due to a fibroma coexisted with pulmonary tuberculosis at both apices. A history of syphilis or stigmata of that disease suggests a gummatous process; Wassermann's test should be applied in every doubtful case. Hydatids must be remembered in patients from Iceland, Shetland, or other localities in which this disease is endemic. The examination of the cerebrospinal fluid may yield data of value. Thus, Gründ has collected eight cases of malignant tumour of the meninges, in seven of which the fluid contained a marked increase of albumin; and Rindfleisch reports three cases of diffuse sarcoma of the meninges in which the fluid obtained on lumbar puncture contained tumour-cells. The age of the patient has some bearing; below forty, according to Schlesinger, tuberculous and gliomatous tumours are the most common medullary growths; whilst of meningeal tumours, lipoma, sarcoma, and hydatid are the forms most often met with; above that age gumma and tubercle are the most common tumours within the cord, solitary sarcoma and psammoma in the meninges.

In the presence of a total paraplegia due to pressure it is impossible to say whether the cord is merely pressed on, or oedematous, or whether there is actual softening or a transverse myelitis.

**Differential Diagnosis.**—Among the various affections which may

resemble a meningeal or medullary tumour, the following deserve special mention:—intercostal neuralgia, sciatica, circumscribed serous meningitis, vertebral tumours, spinal caries, hypertrophic pachymeningitis, spinal syphilis, disseminated sclerosis, combined scleroses of the cord, and syringomyelia.

*Intercostal neuralgia* may be erroneously diagnosed in the early stages. It is, however, characterised by tenderness on pressure over the affected nerves. When intercostal pain is of long duration, and particularly when it is bilateral, symptoms of impaired conduction in the cord are to be most carefully searched for.

*Sciatica* is rarely bilateral. An atrophic palsy or radicular anaesthesia would suggest a vertebral or meningeal growth, and in the presence of these symptoms digital examination of the anterior aspect of the sacrum as an aid in helping to exclude a tumour of the bone should never be omitted.

The *circumscribed serous meningitis* of Krause (29), Oppenheim (39), and Bruns (9), which has been called *hydromeninx* by Auerbach, and described by Sir V. Horsley as chronic spinal meningitis, is in most instances, if not always, indistinguishable from a localised meningeal tumour. Sir V. Horsley states that with one exception all his 27 patients were over puberty; that the pain was not usually limited to one nerve-root, but tended to affect diffuse areas; that in none of his cases was there absolute anaesthesia, and that the sensory impairment was usually slight in degree and not of the dissociated type (*vide* also p. 617).

*Vertebral tumours* cannot always be differentiated; considerable projection of one or more spines in an adult and great pain on movement of the spinal column strongly suggest this diagnosis. The root-pains are usually bilateral from the first. Vertebral tumours are often secondary, meningeal growths primary; hence the detection of a malignant tumour elsewhere renders the former much more probable. Pronounced cachexia for the same reason favours a tumour of the bone. Albumosuria indicates multiple myeloma. Localised oedema over the vertebrae points to malignant disease. Decisive evidence is forthcoming when the tumour projects in the back to either side of the middle line. A skiagram may be conclusive.

*Tuberculous caries of the spine* may give rise to difficulty; a pronounced angular curvature in a young subject is, as Sir W. Gowers points out, almost always due to caries. Root-symptoms are often absent in caries; when present they are usually bilateral and rarely so pronounced as in tumour. The presence of pulmonary tuberculosis is an important point, and a positive tuberculin reaction may also prove of value when the diagnosis lies between a meningeal tumour or spinal caries. A fluctuating tumour in the back or a psoas abscess places the diagnosis beyond doubt. The diagnosis may be impossible in the rare cases of caries in which Brown-Séquard's syndrome is present, and in which there is not any certain evidence of bone disease.

*Hypertrophic pachymeningitis* may be erroneously diagnosed as a menin-

geal tumour (Soltmann, Senator, Collins and Blanchard), and the reverse mistake may be made (Meyer). The circumstance that pachymeningitis usually implicates the cervical enlargement, the bilateral character of the symptoms, the pronounced wasting in the arms, the extensive root-implication before spinal-cord symptoms make their appearance, and the slow course should in most cases permit of a correct diagnosis.

*Chronic myelitis* is a favourite diagnosis. This condition, however, is almost unknown apart from syphilis and the pressure-paraplegias. A. Starr is convinced from a careful review of the literature that in all probability many of the reported cases of subacute or chronic transverse myelitis have been cases of tumour by compression.

*Syphilitic meningo-myelitis* may give rise to error, as in a case of Saenger's which was submitted to operation (46). The coexistence of cerebral manifestations, a history or other evidence of syphilis, the Wassermann reaction, and the effects of treatment will indicate the probable syphilitic nature of the case. But it must be remembered that syphilitic tumours do not always yield to antisiphilitic remedies.

*Disseminated sclerosis* has been erroneously diagnosed (Oppenheim (36), v. Switalski), and in two reported instances this condition was present when a tumour was supposed to exist (Schultze, Nonne). It is especially the spinal form of disseminated sclerosis which gives rise to difficulty in diagnosis. It is stated that multiple neuroma may give rise to a picture almost identical with disseminated sclerosis. A history of pronounced remissions in the course of the case, and such symptoms as a temporary paralysis of a limb, ocular palsy, a fleeting amblyopia or diplopia, giddiness, and the characteristic pallor of the optic discs met with in this disease will establish a diagnosis of disseminated sclerosis, whilst well-marked anaesthesia, root-symptoms, severe pain in the back, and a Brown-Séquard paralysis favour tumour.

*Syringomyelia* has occasionally been mistaken for a meningeal tumour, and operation was indeed undertaken in cases reported by Nonne and by Fürbringer and Hahn. Beevor recorded a case in which syringomyelia was simulated by multiple syphilitic tumours. The diagnosis is especially difficult in cases in which pachymeningitis is associated with syringomyelia. Long duration of the symptoms and lengthy periods during which there is no tendency to progression, absence of root-pains, and the presence of vasomotor and trophic disturbances, of pronounced scoliosis, nystagmus, spina bifida occulta, and various other congenital abnormalities are characteristic of syringomyelia. The distressing flexor spasms so common in tumour are not seen in this disease (Oppenheim).

*Tubes dorsalis* was simulated in a case described by Hughes Bennett, in which numerous tumours grew from the posterior nerve-roots.

**Prognosis.**—Until 1888, when Sir W. Gowers and Sir V. Horsley proved that a spinal tumour might be successfully dealt with by the surgeon, the outlook was most dismal, for the only growths benefited by medicinal treatment are the syphilitic. Analogy suggests that tuberculous tumours and hydatids may cease to grow. Henschen has



described the case of a man with multiple subcutaneous neuromas, who presented symptoms pointing to a tumour of the cord but subsequently improved gradually. Oppenheim refers to a case in which a tumour was diagnosed, and an operation under consideration, when the patient was attacked by an acute febrile disease, in the course of which there was marked improvement. It is probable that the cases of tumour occasionally recorded, in which symptoms disappeared, were incorrectly diagnosed; possibly they were instances of localised serous meningitis. As regards duration of life, Sir W. Gowers (22) states that in the majority of cases of meningeal tumour death ensues in from one to three years from the onset of symptoms, but that the duration is longer in extradural than in intradural growths. Bruns estimates the duration in extradural growths as one year one month, in intradural tumours as two years three months. The average duration of life in spinal tumour according to Schlesinger's analysis of 224 cases is as follows:—intra-medullary=20 months; intradural=33·59 months; extradural=17·2 months; vertebral=10 months.

**Treatment.**—Antisymphilitic treatment is indicated in every case of spinal tumour of uncertain nature, unless, as Sir W. Gowers puts it, there has been no *possibility* of syphilitic infection. Potassium iodide should be given in doses of at least 40 grains, three times a day, and mercury administered every second day by inunction or intramuscular injection until salivation is produced. If after a month's medicinal treatment (Gowers) there has not been distinct improvement, operation with the object of removing the tumour should be carried out without delay, should the case appear suitable for this procedure.

In *medullary tumours* little can be expected from surgical intervention, since these growths are usually diffuse, and when circumscribed are almost always deeply situated, whilst even if recognisable on the surface their excision will almost inevitably produce much damage to the cord. Distinct improvement has nevertheless occasionally followed laminectomy, a result possibly explained by relief of pressure. Dana has suggested that in a case of complete paraplegia with nerve pain, when a localised primary medullary sarcoma is found at operation, the portion of cord including the growth might with advantage be excised. This operation has not, so far as I know, been carried out in actual practice.

*Meningeal tumours* offer a very different outlook to the surgeon, for they are often simple, of small size, loosely adherent, usually situated on the lateral or posterior aspect of the cord, and easily removed if correctly located. Sir W. Gowers and Sir V. Horsley in 1888 demonstrated that it was possible to remove a meningeal tumour with ultimate complete recovery from the paraplegia which it had produced. They stated that intradural tumours are almost always operable. Collins concludes from collected post-mortem evidence that at least 50 per cent of meningeal tumours are removable, and Allen Starr places the percentage as high as 75. The results of operation support these opinions; Bruns in 1895 collected 13 recorded cases in which an operation had

been performed; in 4 of which there had been marked improvement or cure, in 1 slight improvement, and in 8 death. Two years later the same author collected 20 cases, in 6 of which (30 per cent) there had been pronounced improvement. Cushing reviewed the literature up to 1904. Schultze in 1905 refers to 62 cases which had been operated upon, in 38 per cent of which cure or considerable improvement had resulted. Dr. R. T. Williamson in 1907 collected 51 successful cases from the literature. The personal experience of individual observers is especially instructive. Oppenheim up to 1907 had advised operation in 12 cases, 7 with a successful and 5 with a fatal result. The fatal cases with one exception occurred early in the series, and 5 of the successful cases were operated on during the year preceding the publication of his results. Schultze, writing in the same year, stated that of 13 cases operated upon 6 had completely recovered and 1 was permanently relieved. I understand that Oppenheim has now (1909) recommended operation in 26 cases, in 10 of which there has been complete recovery, and in 3 pronounced improvement. The conclusion is therefore justified that in the hands of surgeons who have had special experience in dealing with these cases, 50 per cent of meningeal tumours submitted to operation can be removed with eventual recovery. Operation is not, however, to be confined to cases in which the diagnosis of a localised meningeal tumour is beyond question. Indeed, the practically unanimous opinion at an important discussion in Berlin in 1906 upon the surgical treatment of spinal tumours was that, if after consideration in a doubtful case, the disease is observed to be progressive, and the existence of a meningeal tumour is at all probable, an exploratory laminectomy should be undertaken. In these circumstances operation should only be advised if the level of the growth can be accurately localised. In a certain proportion of cases a circumscribed serous meningitis, caries of the bone, a vertebral or medullary tumour will be met with. The first condition will probably be greatly benefited or cured, and no harm will necessarily follow in those subsequently named. Although the results of Sir V. Horsley, Krause, and others indicate that the mortality of exploratory laminectomy is not heavy in the hands of experts (Sir V. Horsley states that his first twenty operations for chronic spinal meningitis were performed without a death), yet this is a factor which cannot be ignored in arriving at a decision in a doubtful case.

The literature of the surgical treatment of tumours of the cauda equina has been recently reviewed by Cassirer. Among 24 cases in which operation had been attempted, in only 3 was it successful. In the discussion following Cassirer's paper the information was elicited that 2 of these cases had relapsed. The reasons for failure are the circumstances that in this situation tumours are often malignant, multiple, or of large size, and at the same time difficult to localise.

If operation is decided upon there should be no delay provided that the growth can be localised, for, as Sir V. Horsley points out, delay can only cause harm. The signs of a total transverse lesion do not contra-

indicate operative interference, since the symptoms may be a mere consequence of pressure unaccompanied by structural damage. Recovery may follow the removal of the tumour notwithstanding the presence of cystitis and bed-sores.

The risks of operation are no doubt greater when the tumour lies opposite the upper cervical segments; but in several reported instances a meningeal growth has been successfully removed from this region (Putnam, Brodnitz, and others). The dura should always be opened when a tumour is not found upon its outer surface, otherwise many intradural growths will escape detection (38). Krause advocates incision of the dura even when an extradural tumour is exposed, for in one of his cases there was a second tumour within the dural sheath. A fatal termination soon after operation may be due to collapse or sepsis, at a later date to general debility often associated with bed-sores and cystitis, to multiple growths, or coexisting disease. A localised myelitis or it may be injury to the cord during operation explains those cases in which no improvement follows the removal of the tumour.

Oppenheim (40) has recently discussed the progress of recovery after removal of meningeal tumours. Improvement is often very rapid at first, but subsequently may be very slow. Relapses are apt to occur, especially towards the end of the first or during the second and third weeks. The duration of convalescence varies considerably; in one of Oppenheim's cases the patient was perfectly well within two months, but as a rule recovery is not complete for six months, and improvement may take much longer, even continuing during the second year. Some spasticity often remains for a considerable time after power in the lower limbs has been completely regained.

The symptomatic treatment of meningeal and medullary tumours is very similar to that of other forms of chronic paraplegia. Great care must be taken to avoid bed-sores; bladder symptoms and cystitis should be treated on general principles; and for the relief of pain recourse may be had to antipyrin, aspirin, or some of the other analgesics.

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